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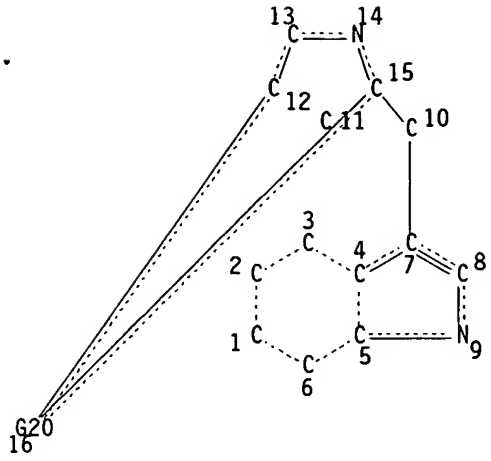
L1 STR



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GRAPH ATTRIBUTES:
RING(S) ARE ISOLATED OR EMBEDDED
NUMBER OF NODES IS 16

STEREO ATTRIBUTES: NONE
L3 559 SEA FILE=REGISTRY SSS FUL L1

100.0% PROCESSED 13578 ITERATIONS 559 ANSWERS
SEARCH TIME: 00.00.29

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FILE COVERS 1967 - 6 Jan 1996 VOL 124 ISS 2
FILE LAST UPDATED: 6 Jan 1996 (960106/ED)

To help control your online searching costs, consider using the HCAplus file when using the FSEARCH command or when conducting SmartSELECT searches with large numbers of terms.

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L4          126 L3

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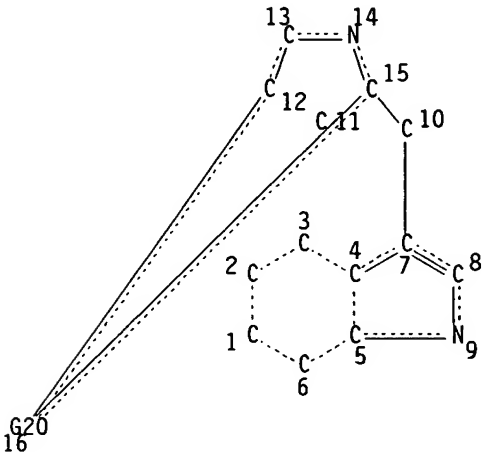


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DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
RING(S) ARE ISOLATED OR EMBEDDED
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STEREO ATTRIBUTES: NONE
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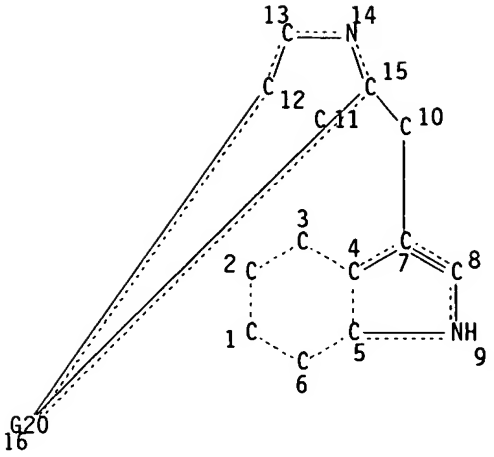

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DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
RING(S) ARE ISOLATED OR EMBEDDED
NUMBER OF NODES IS 16

STEREO ATTRIBUTES: NONE
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100.0% PROCESSED 559 ITERATIONS 536 ANSWERS
SEARCH TIME: 00.00.05

=> fil caplus
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USE IS SUBJECT TO THE TERMS OF YOUR CUSTOMER AGREEMENT

FILE COVERS 1967 - 6 Jan 1996 VOL 124 ISS 2
FILE LAST UPDATED: 6 Jan 1996 (960106/ED)

To help control your online searching costs, consider using the
HCAplus file when using the FSEARCH command or when conducting

SmartSELECT searches with large numbers of terms.

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=> s l6
L7          124 L6

=> d 1-20 cbib abs hitrn
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L7 ANSWER 1 OF 124 CAPLUS COPYRIGHT 1996 ACS
1995:987946 Preparation of [(triazolyl)indolyl]methylpyrrolidines as 5-HT1-like agonists.. Matassa, Victor Giulio; Sternfeld, Francine; Street, Leslie Joseph (Merck Sharp and Dohme Ltd., UK). PCT Int. Appl. WO 9521167 A1 950810, 22 pp. DESIGNATED STATES: W: AM, AT, AU, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, JP, KE, KG, KP, KR, KZ, LK, LR, LT, LU, LV, MD, MG, MN, MW, MX, NL, NO, NZ, PL, PT, RO, RU, SD, SE, SI, SK, TJ, TT, UA, US; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, DE, DK, ES, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG. (English). CODEN: PIXXD2. APPLICATION: WO 95-GB135 950124. PRIORITY: GB 94-2011 940202.

AB Title compds. (I; R = H, C1-6 alkyl), were prepd. Thus, 4'-(1,2,4-triazol-4-yl)phenylhydrazine and (2S)-N-tert-butoxycarbonyl-3-(pyrrolidin-2-yl)propanal were stirred in 4% aq. H2SO4 at room temp.-reflux to give 34% I (R = H), isolated as the oxalate. I showed pEC50 .gtoreq.5.0 in a test of their ability to mediate contraction of the saphenous vein of rabbits.

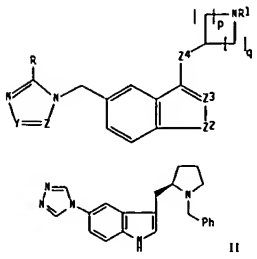
IT RN LIST MAY NOT BE COMPLETE: 154594-16-8 171550-13-3
171550-14-4 171550-15-5 171550-16-6
171752-92-4

L7 ANSWER 2 OF 124 CAPLUS COPYRIGHT 1996 ACS (Continued)
(prepn. of triazole derivs. as serotoninergic agonists)

IT 171182-32-4P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)
(prepn. of triazole derivs. as serotoninergic agonists)

L7 ANSWER 2 OF 124 CAPLUS COPYRIGHT 1996 ACS
1995:969448 Document No. 124:8823 Preparation of triazole derivatives as serotoninergic agonists. Matassa, Victor Giulio; Sternfeld, Francine; Street, Leslie Joseph (Merck Sharp and Dohme Ltd., UK). PCT Int. Appl. WO 9521166 A1 950810, 49 pp. DESIGNATED STATES: W: AM, AT, AU, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, JP, KE, KG, KP, KR, KZ, LK, LR, LT, LU, LV, MD, MG, MN, MW, MX, NL, NO, NZ, PL, PT, RO, RU, SD, SE, SI, SK, TJ, TT, UA, US; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, DE, DK, ES, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG. (English). CODEN: PIXXD2. APPLICATION: WO 95-GB134 950124. PRIORITY: GB 94-2016 940202.

GI



I

II

AB Title compds. [I; R = H, hydrocarbyl, heterocyclyl, etc.; R1 = cycloalkyl, alkoxyalkyl, aryl(alkyl), etc.; 1 of Y,Z = N and the other = (un)substituted CH; Z1 = bond, alkylene; Z2 = O, S, (alkyl)imino; Z3 = N, (alkyl-substituted)CH; Z4 = alkylene; p = 0 or 1; q = 1-4; p+q = 2-4], agonists of 5-HT1-like receptors, were prepd. Thus, (2R)-N-tert-butoxycarbonylpyrrolidine-2-propanal was cyclocondensed with 4-(1,2,4-triazol-4-yl)phenylhydrazine (prepn. each given) and the product condensed with PhCHO to give title compd. II. I had pEC50 of .gtoreq.5.0 for contraction of rabbit saphenous vein.

IT 171182-20-0P 171182-21-1P 171182-22-2P
171182-23-3P 171182-24-4P 171182-25-5P
171182-26-6P 171182-27-7P 171182-28-8P
171182-29-9P 171182-30-2P 171182-31-3P
RL: BAC (Biological activity or effector, except adverse); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

L7 ANSWER 3 OF 124 CAPLUS COPYRIGHT 1996 ACS
1995:933846 Document No. 124:688 The in vivo pharmacological profile of a 5-HT1 receptor agonist, CP-122,288, a selective inhibitor of neurogenic inflammation. Gupta, P.; Brown, D.; Butler, P.; Ellis, P.; Grayson, K. L.; Land, G. C.; Macor, J. E.; Robson, S. F.; Wythes, M. J.; Shepperson, N. B. (Departments of Discovery Biology and Discovery Chemistry, Pfizer Central Research, Sandwich, Kent, CT13 9NJ, UK). Br. J. Pharmacol., 116(5), 2385-90 (English) 1995. CODEN: BJPCBM. ISSN: 0007-1188.

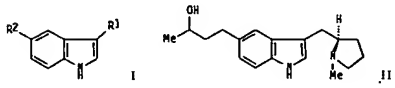
AB The aim of the present study was to investigate the in vivo pharmacol. profile of CP-122,288, an indole-deriv. with a conformationally restricted N-methylpyrrolidinyl basic side chain in the C-3 position. This C-3 substituent structurally differentiates CP-122,288 from the 5-HT1D receptor agonist sumatriptan, which possesses an N,N-dimethylaminoethyl group. When administered prior to elec. stimulation of the trigeminal ganglion, CP-122,288 (0.3-300 ng kg-1, i.v.) produced a dose-related inhibition of plasma protein extravasation in rat dura mater (min. ED, MED, 3 ng kg-1 i.v., P < 0.05; maximal inhibition of plasma extravasation at 30 ng kg-1 i.v., P < 0.01). Sumatriptan produced a similar inhibition of plasma leakage in the dura, but at much higher dose levels (MED, 100 .mu.g kg-1 i.v., P < 0.05). Thus, CP-122,288 is of the order of 104 fold more potent than sumatriptan. At all doses tested, CP-122,288 did not inhibit plasma protein extravasation measured in extracranial tissues such as the lower lip, eyelid, and conjunctiva. In a sep. series of studies in the anesthetized rat, CP-122,288 (0.003-3 .mu.g kg-1 i.v.) produced no change in either heart rate or mean arterial blood pressure, thus demonstrating that doses of CP-122,288 which inhibit plasma protein leakage in rat dura, are devoid of hemodynamic effects. Following a 5 min period of elec. stimulation of the trigeminal ganglion, a 20 min period of sustained neurogenically-driven plasma extravasation, occurring in the absence of elec. stimulation, was initiated. By administration of the compd. 5 min after completing the phase of elec. stimulation, this protocol permitted the evaluation of the activity of CP-122,288 on the ongoing and established inflammatory event. CP-122,288 (30 and 300 ng kg-1, i.v. P <0.01 and P <0.05, resp.) produced a complete inhibition of plasma protein leakage which was consistent with its effects when administered prior to trigeminal ganglion stimulation. In the anesthetized dog, CP-122,288 and sumatriptan, at 1-300 .mu.g kg-1, i.v., produced a dose-dependent redn. in carotid arterial blood flow and coronary arterial diam. These data demonstrate that sumatriptan inhibits neurogenic inflammation in the rat (MED, 100 .mu.g kg-1, i.v.) and produces vasoconstriction in the dog, over a similar dose-range. Interestingly, doses of CP 122,288 that inhibit neurogenic inflammation in rat dura mater (0.3-300 ng kg-1) were demonstrated to be devoid of vasoconstrictor activity in either the carotid or coronary vascular beds of dog. These data demonstrate that in the rat, CP-122,288 is a highly potent and selective inhibitor of neurogenic inflammation in intracranial tissues, at doses which are devoid of vasoconstrictor activity in dog. Potentially, CP-122,288 may be of use for the acute treatment of migraine, without the risk of cardiovascular side-effects.

IT 143321-74-0, CP-122288
RL: ADV (Adverse effect, including toxicity); BAC (Biological activity or effector, except adverse); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

L7 ANSWER 3 OF 124 CAPLUS COPYRIGHT 1996 ACS (Continued)
(CP-122,288 pharmacol. profile as selective inhibitor of neurogenic inflammation in relation to migraine treatment)

L7 ANSWER 4 OF 124 CAPLUS COPYRIGHT 1996 ACS
1995:772570 Document No. 123:169499 Indole derivatives as 5-HT1-like agonists for use in migraine. Wythes, Martin James (Pfizer Ltd., UK; Pfizer Inc.; Pfizer Research and Development Company, N.V./S.A.). PCT Int. Appl. WO 9424127 A1 941027, 124 pp. DESIGNATED STATES: W: AU, BR, CA, CN, CZ, FI, HU, JP, KR, NO, NZ, PL, RU, US; RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE. (English). CODEN: PIXXD2. APPLICATION: WO 94-EP1121 940411. PRIORITY: GB 93-8360 930422; GB 93-24433 931127.

GI



AB The title compds., 3-(pyrrolidinylmethyl)indoles and 3-(piperidinylmethyl)indoles I [R1 = (2-pyrrolidinyl)methyl, 3-pyrrolidinyl, 4-piperidinyl, (3-piperidinyl)methyl; R2 = alkyl, oxoalkyl, etc.] were disclosed as selective 5-HT1-like agonists useful in the treatment of migraine, cluster headache, chronic paroxysmal hemicrania and headache assocd. with vascular disorders. A specifically claimed example compd. is 5-(3-hydroxybutyl)-3-[(R)-(1-methyl-2-pyrrolidinyl)methyl]-1-H-indole (II).

IT 143322-56-9
RL: RCT (Reactant)
(prepn. of (pyrrolidinyl)indoles 5-HT1-like agonists)

IT 143322-57-0
RL: RCT (Reactant)
(prepn. of (pyrrolidinylmethyl)indoles 5-HT1-like agonists)

IT 143322-46-7P 153435-71-3P 153435-73-5P
153525-35-0P 153525-50-9P 153525-51-0P
167303-50-6P 167303-51-7P 167303-54-0P
167303-55-1P 167303-56-2P 167303-63-1P
167303-64-2P 167303-66-4P 167303-67-5P
167303-71-1P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)
(prepn. of (pyrrolidinylmethyl)indoles 5-HT1-like agonists)

IT 167302-44-5P 167302-45-6P 167302-46-7P
167302-47-8P 167302-48-9P 167302-49-0P
167302-50-3P 167302-51-4P 167302-52-5P
167302-53-6P 167302-54-7P 167302-55-8P
167302-56-9P 167302-62-7P 167302-63-8P
167302-64-9P 167302-65-0P 167302-66-1P
167302-71-8P 167302-72-9P 167302-73-0P
167302-74-1P 167302-75-2P 167302-76-3P
167302-77-4P 167302-78-5P 167302-79-6P
167302-80-9P 167302-81-0P 167302-82-1P
167302-83-2P 167302-84-3P 167302-92-3P

L7 ANSWER 4 OF 124 CAPLUS COPYRIGHT 1996 ACS (Continued)
167302-93-4P 167302-94-5P 167302-95-6P
167302-96-7P 167302-97-8P 167302-98-9P
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167303-48-2P 167303-49-3P 167303-53-9P
167303-57-3P
RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of (pyrrolidinylmethyl)indoles 5-HT1-like agonists)

L7 ANSWER 5 OF 124 CAPLUS COPYRIGHT 1996 ACS
1995:685346 Document No. 123:313894 Z+Y-ZH compounds as potential 1,3-dipoles. Part 44. Asymmetric 1,3-dipolar cycloaddition reactions of imines and chiral cyclic dipolarophiles. Cooper, Daniel M.; Grigg, Ronald; Hargreaves, Simon; Kennewell, Peter; Redpath, James (Sch. Chem., Leeds Univ., Leeds, LS2 9JT, UK). Tetrahedron, 51(28), 7791-808 (English) 1995. CODEN: TETRAB. ISSN: 0040-4020.

AB Metallo-1,3-dipoles generated in situ from both aryl and aliph. imines of .alpha.-amino esters by the action of silver salts and tertiary amines undergo cycloaddn. at room temp. to give (menthyl)furo[3,4-c]pyrrolecarboxylates pyrrolopyrrolecarboxyates. .pi.-Interaction between the dipolarophile carbonyl group and the aryl group in the aryl imines is not required for good induction. The stronger the base the faster the cycloaddn. with 2-t-butyl-1,1,3,3-tetramethylguanidine > DBU > NEt3. X-ray crystal structures of representative cycloadducts established the abs. configuration of the pyrrolidine stereocenters.

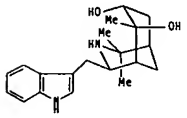
IT 170027-89-1P 170027-95-9P
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of)

L7 ANSWER 6 OF 124 CAPLUS COPYRIGHT 1996 ACS
1995:575044 Document No. 122:309995 Differentiating Penicillium species by detection of indole metabolites using a filter paper method. Lund, F. (Department of Biotechnology, Technical University of Denmark, Lyngby, Den.). Lett. Appl. Microbiol., 20(4), 228-31 (English) 1995. CODEN: LAMIE7. ISSN: 0266-8254.
AB The indole secondary metabolites chaetoglobosin C, cyclopiazonic acid, isofumigaclavine A and rugulovasine A and B produced by several Penicillium species growing on Czapek yeast autolyzate agar were detected directly in the culture using filter paper wetted with Ehrlich reagent dissolved in ethanol. The filter paper was placed on the mycelial side of an agar plug and the metabolites were visualized as a violet zone on the paper within 10 min. It was shown that the combined characters of the violet reaction on filter paper and the ability to grow on creatine sucrose agar occurred in 5 out of 16 species of Penicillium exmd. A few addnl. simple morphol. and physiol. criteria were then sufficient for identification of P. camemberti, P. commune, P. discolor, P. expansum and P. roueforti var. rouqueforti.
IT 50645-76-6, Chaetoglobosin C
RL: ANT (Analyte); ANST (Analytical study)
(Differentiating Penicillium species by detection of indole metabolites using a filter paper method)

L7 ANSWER 7 OF 124 CAPLUS COPYRIGHT 1996 ACS
1995:549880 Document No. 122:306133 Effect of a 5-HT1 receptor agonist, CP-122,288, on edema formation induced by stimulation of the rat saphenous nerve. Kajekar, Radhika; Gupta, Paul; Shepperson, Nicholas B.; Brain, Susan D. (Vascular Biology Research Centre, King's College, London, SW3 6LX, UK). Br. J. Pharmacol., 115(1), 1-2 (English) 1995. CODEN: BJPCBM. ISSN: 0007-1188.
AB Neurogenic edema formation in the rat hind paw skin induced by elec. stimulation of the saphenous nerve and measured by extravasation of [125I]-albumin, was inhibited by the 5-HT1B receptor agonist, CP-93,129, and the novel tryptamine analog, CP-122,288. Significant inhibition of up to 66% of control was obsd. with CP-122,288 (2 .times. 10-14 - 2 .times. 10-7 mol kg-1) and CP-93,129 (5 .times. 10-7-5 .times. 10-6 mol kg-1), with the min. ED for CP-122,288 being about 107 fold less than that for CP-93,129. Edema formation induced by the intradermal administration of exogenous mediators (substance P and histamine) in rat dorsal skin was not inhibited by CP-122,288 (2 .times. 10-10 mol kg-1). These results suggest that CP-122,288 is a potent inhibitor of neurogenic inflammation in rat skin and that the effect may be due to a prejunctional inhibition of neuropeptide release.
IT 143321-74-8, CP-122288
RL: BAC (Biological activity or effector, except adverse); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(neurogenic edema inhibition by 5-HT1 receptor agonist CP-122288)

L7 ANSWER 8 OF 124 CAPLUS COPYRIGHT 1996 ACS
1995:521096 Document No. 122:310000 High-performance liquid chromatography comparison of supercritical-fluid extraction and solvent extraction of microbial fermentation products. Cocks, Simon; Wrigley, Stephen K.; Chicarelli-Robinson, M. Ines; Smith, Roger M. (Xenova Ltd, 240 Bath Road, Slough Berkshire, SL1 4EQ, UK). J. Chromatogr., A, 697(1 + 2), 115-22 (English) 1995. CODEN: JCRAEY.
AB The use of supercrit. fluids for the extn. of biol. active compds. from the biomass of microbial ferms. has been compared with extn. using the org. solvents methanol and dichloromethane. Compds. representing a range of structural types were selected for investigation. All the exts. obtained were exmd. by reversed-phase HPLC. The extractability of metabolites using unmodified and methanol-modified supercrit.-fluid carbon dioxide was exmd. in particular detail for six microbial metabolites: chaetoglobosin A, mycolutein, luteoreticulin, 7,8-dihydro-7,8-epoxy-1-hydroxy-3-hydroxymethylxanthone-8-carboxylic acid Me ester, sydowinin B and elaiophylin. The extn. strength of supercrit.-fluid carbon dioxide alone appeared to be lower than that of dichloromethane. All the components of interest that were extractable with dichloromethane and methanol were also extractable with methanol-modified carbon dioxide.
IT 50335-03-0P, Chaetoglobosin A
RL: PUR (Purification or recovery); PREP (Preparation)
(HPLC comparison of supercrit.-fluid vs. solvent extn. of microbial ferm. products)

L7 ANSWER 9 OF 124 CAPLUS COPYRIGHT 1996 ACS
1995:517652 Document No. 123:33479 Synthesis of Aristotelia-type alkaloids. Part XV. Total synthesis of (+)-hobartinol. Dobler, Markus; Anderson, James C.; Juch, Mathias; Borschberg, Hans-Juerg (Lab. Org. Chem., Eidgenoessischen Tech. Hochschule, Zurich, CH-8092, Switz.). Helv. Chim. Acta, 78(2), 292-300 (English) 1995. CODEN: HCACAV. ISSN: 0018-019X.
GI



I

AB Synthetic (+)-makomakine was transformed in six steps into (+)-(17R,18R)-17,18-dihydrohobartine-17,18-diol ((+)-I) with an overall yield of 36%. This compd. was shown to be identical with natural hobartinol, a monoterpene indole alkaloid from Aristotelia australasica, originally believed to be the (17S)-epimer. At the same time, the synthesis of (+)-I delineates the hitherto unknown abs. configuration of this metabolite.
IT 163812-32-6P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)
(total synthesis of hobartinol)

L7 ANSWER 10 OF 124 CAPLUS COPYRIGHT 1996 ACS
1995:466381 Document No. 122:256183 The pre- and postjunctional activity of CP-122,288, a conformationally restricted analog of sumatriptan. Beattie, David T.; Connor, Helen E. (Pharmacology II, Glaxo Research and Development Ltd., Park Road, Ware Herts, SG12 0DP, UK). Eur. J. Pharmacol., 276(3), 271-6 (English) 1995. CODEN: EJPHAZ. ISSN: 0014-2999.

AB The present study investigated the pre- and postjunctional activity of CP-122,288 (5-methyl-aminosulfonylmethyl-3-(N-methylpyrrolidin-2R-yl-methyl)-1H -indole), an analog of the vascular 5-HT1 receptor agonist, sumatriptan. CP-122,288 inhibited neurogenic plasma protein extravasation in rat dura with a potency approx. 40 000-fold greater than sumatriptan (ID50 values of 0.3 pmol/kg and 13.9 nmol/kg i.v. resp.). However, CP-122,288 was only approx. 2-fold more potent than sumatriptan at inhibiting neurogenically mediated contractions of the dog saphenous vein. CP-122,288 contracted the dog saphenous vein and basilar artery with a potency approx. 2-fold greater than that of sumatriptan. Both compds. possessed similar affinities at either human 5-HT1D.alpha. or 5-HT1D.beta. receptors. It is concluded that CP-122,288 exhibits a prejunctional selectivity in the meninges to inhibit dural plasma protein extravasation independent of 5-HT1D.alpha. and 5-HT1D.beta. receptor activation.

IT 143321-74-8, CP-122288
RL: BAC (Biological activity or effector, except adverse); BIOL (Biological study)
(pre- and postjunctional activity of CP-122,288, a conformationally restricted analog of sumatriptan)

L7 ANSWER 11 OF 124 CAPLUS COPYRIGHT 1996 ACS
1995:421524 Document No. 122:205025 Suppression by the sumatriptan analog, CP-122,288 of c-fos immunoreactivity in trigeminal nucleus caudalis induced by intracisternal capsaicin. Cutrer, F. Michael; Schoenfeld, David; Limmroth, Volker; Panahian, Nariman; Moskowitz, Michael A. (Harvard Med. Sch., Massachusetts Gen. Hosp., Boston, MA, 02114, USA). Br. J. Pharmacol., 114(5), 987-92 (English) 1995. CODEN: BJPCBM. ISSN: 0007-1188.

AB The effects of an i.v. administered sumatriptan analog were exmd. on c-fos-like immunoreactivity (c-fos-LI), a marker of neuronal activation, evoked within trigeminal nucleus caudalis (TNC) and other brain stem regions 2 h after intracisternal injection of the irritant, capsaicin (0.1 nn, 0.1 nM), in pentobarbitone-anesthetized Hartley guinea pigs. C-fos-LI was assessed in eighteen serial sections (50 .mu.m) using a polyclonal antiserum. A weighted av., reflecting total expression within lamina I, IIO of TNC was obtained from three representative levels (i.e., at -0.225 nn, -2.475 nn and -6.075 nn). Capsaicin caused significant labeling within lamina I, IIO, a region contg. axonal terminatns of small unmyelinated C-fibers, as well as within the nucleus of the solitary tract, area postrema and medial reticular nucleus. A similar distribution of pos. cells was reported previously after intracisternal injection of other chem. irritants such as autologous blood or carrageenin. Pretreatment with a conformationally restricted sumatriptan analog (with some selectivity for 5-HT1B and 5-HT1D receptor subtypes) CP-122,288, reduced the weighted av. by approx. 50-60% ($P < 0.05$) in lamina I, IIO at 100 pmol kg-1, i.v., but did not decrease cell no. within area postrema, nucleus of the solitary tract or medical reticular nucleus. A similar pattern was reported previously following sumatriptan, dihydroergotamine or CP-93,129 administration after noxious meningeal stimulation. We conclude that modifications at the amino-Et side chain of sumatriptan dramatically enhance the suppression of c-fos expression within TNC, a finding consistent with its remarkable potency against neurogenic plasma protein extravasation within dura matter. CP-122,288 and related analogs may serve as an important prototype for drug development in migraine and related headaches.

IT 143321-74-8, CP-122288
RL: BAC (Biological activity or effector, except adverse); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(suppression by sumatriptan analog, CP-122,288 of c-fos immunoreactivity in trigeminal nucleus caudalis induced by intracisternal capsaicin)

L7 ANSWER 12 OF 124 CAPLUS COPYRIGHT 1996 ACS
1995:354225 Document No. 122:133200 5-arylindole derivatives and their use as serotonin (5-HT1) agonists. Macor, John Eugene (Pfizer Inc., USA). PCT Int. Appl. WO 9410171 A1 940511, 72 pp. DESIGNATED STATES: W: AU, BR, CA, CZ, JP, KR, NO, NZ, PL, RU, US; RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE. (English). CODEN: PIXXDZ. APPLICATION: WO 93-US9790 931019. PRIORITY: US 92-970758 921102.

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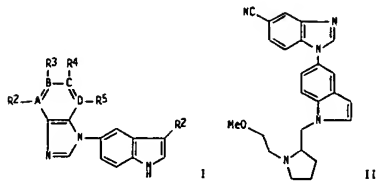

AB The title compds. I (R1 = aminoalkyl; R2-R5 = H, alkyl, aryl, etc.) were disclosed. I are useful in treating migraine and other disorders; they are useful psychotherapeutics and are potent serotonin (5-HT1) agonists and benzodiazepine agonists and antagonists and may be used in the treatment of depression, anxiety, eating disorders, obesity, drug abuse, cluster headache, migraine, pain and chronic paroxysmal hemicrania and headache assocd. with vascular disorders, and other disorders arising from deficient serotonergic neurotransmission. I are also useful as centrally acting antihypertensives and vasodilators. A specifically claimed example compd. is 5-cyano-1-[[3-[1-(2-methoxyethyl)-2-pyrrolidinyl]methyl]-5-indolyl]-1H-benzimidazole (II).

IT 160907-04-0P 160907-05-1P 160907-06-2P
160907-07-3P
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of)

IT 143322-01-4P 151272-89-8P 151272-90-1P
151272-99-0P 151273-00-6P 151273-01-7P
151273-05-1P 151273-06-2P 151273-07-3P
151273-08-4P 151273-11-9P 158752-53-5P
160906-44-5P 160906-45-6P 160906-46-7P
160906-47-8P 160906-48-9P 160906-49-0P
160906-50-3P 160906-51-4P 160906-54-7P
160906-55-8P 160906-81-0P 160906-82-1P
160906-83-2P 160906-84-3P 160906-85-4P
160906-86-5P 160906-87-6P 160906-95-6P
160906-96-7P 160906-97-8P 160907-00-6P
160907-08-4P
RL: SPN (Synthetic preparation); PREP (Preparation)

L7 ANSWER 12 OF 124 CAPLUS COPYRIGHT 1996 ACS (Continued)
(prepn. of, as intermediate for arylindole serotoninergic agonist)

IT 160906-56-9P 160906-57-0P 160906-58-1P
160906-59-2P 160906-60-5P 160906-61-6P
160906-62-7P 160906-63-8P 160906-64-9P
160906-65-0P 160906-66-1P 160906-68-3P
160906-69-4P 160906-72-9P 160906-73-0P
160906-74-1P 160906-75-2P 160906-79-6P
160906-80-9P 160906-91-2P 160906-94-5P
160907-03-9P
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of, as serotoninergic agonist)

IT 151272-88-7
RL: RCT (Reactant)
(reactant for arylindole serotoninergic agonist)

IT 143321-69-1 151273-49-3 160907-09-5
RL: RCT (Reactant)
(serotoninergic agonist)

L7 ANSWER 13 OF 124 CAPLUS COPYRIGHT 1996 ACS
1995:300051 Document No. 122:64328 Use of indole derivatives as 5-HT1 antagonists. Macor, John Eugene (Pfizer Inc., USA). PCT Int. Appl. WO 9425023 A1 941110, 22 pp. DESIGNATED STATES: W: AU, BG, BR, CA, CN, CZ, FI, HU, JP, KR, NO, NZ, PL, RO, RU, SK; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, DE, DK, ES, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG. (English). CODEN: PIXXD2. APPLICATION: WO 94-IB79 940426. PRIORITY: US 93-53930 930427.

AB The present invention relates to pharmaceutical compns. contg. (R)-5-(methylaminosulfonylmethyl)-3-(N-methylpyrrolidin-2-ylmethyl)-1H-indole or (R)-5-(methylaminosulfonylmethyl)-3-(pyrrolidin-2-ylmethyl)-1H-indole for the treatment of conditions such as hypertension, depression, anxiety, eating disorders, obesity, drug abuse, cluster headache, migraine, pain, chronic paroxysmal hemicrania, and headache assocd. with vascular disorders.

IT 143321-82-8P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)
(indole derivs. for treatment of disorders from deficient serotonergic neurotransmission)

IT 143321-74-8P 143321-78-2P
RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(indole derivs. for treatment of disorders from deficient serotonergic neurotransmission)

L7 ANSWER 14 OF 124 CAPLUS COPYRIGHT 1996 ACS
1995:191714 Document No. 122:106219 Synthesis of Aristotelia-type alkaloids. Part XIV. total synthesis of (+)-aristolone. Dobler, Markus; Borschberg, Hans-Juerg (Lab. Org. Chem., Eidgenoessischen Technischen Hochschule, Zurich, CH-8092, Switz.). Tetrahedron: Asymmetry, 5(10), 2025-32 (English) 1994. CODEN: TASYE3. ISSN: 0957-4166. OTHER SOURCES: CASREACT 122:106219.

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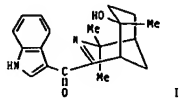

I

AB The first total synthesis of the highly functionalized monoterpenoid indole alkaloid (+)-aristolone (I) is described. This investigation uncovered the hitherto unknown relative and abs. configuration of this rare metabolite which had been isolated before by others in ppa-amts. from Aristotelia australasica. Dehydration of synthetic I led to a readily separable mixt. of the two alkaloids 11,12-didehydro-1-oxonakonakine and 11,12-didehydro-1-oxohobartine which had been isolated in 1988 from A. chilensis.

IT 159979-26-7P
RL: SPN (Synthetic preparation); PREP (Preparation)
(total synthesis of aristolone)

L7 ANSWER 15 OF 124 CAPLUS COPYRIGHT 1996 ACS
1994:681120 Document No. 121:281120 The synthesis of .alpha.-(3-indolylmethyl)proline-containing compounds as CCK ligands: analogs of PD-134308. Kendrick, David A.; Ryder, Hamish; Semple, Graeme; Sheppard, Andrew; Szelke, Michael (Res. Cent., Southampton Univ., Southampton, SO1 7NP, UK). Pept. 1992, Proc. Eur. Pept. Symp., 22nd, Meeting Date 1992, 579-80. Editor(s): Schneider, Conrad H.; Eberle, Alex N. ESCOM: Leiden, Neth. (English) 1993. CODEN: 60LUAN.

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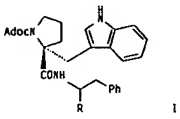

I

AB A report from a symposium on the stereoselective prepn. of analogs I (Adoc = 2-adamantyloxycarbonyl) which have and .alpha.-(3-indolylmethyl)proline residue in place of the .alpha.-methyl-D-tryptophan of PD 134308.

IT 158873-11-1DP, peptides contg.
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)
(asym. synthesis of .alpha.-(3-indolylmethyl)proline-contg. peptides as analogs of PD 134308)

IT 158873-12-2DP, derivs.
RL: SPN (Synthetic preparation); PREP (Preparation)
(asym. synthesis of .alpha.-(3-indolylmethyl)proline-contg. peptides as analogs of PD 134308)

L7 ANSWER 16 OF 124 CAPLUS COPYRIGHT 1996 ACS
1994:680497 Document No. 121:280497 Use of 2,5-Dimethylpyrrole as an Amino-Protecting Group in an Efficient Synthesis of 5-Amino-3-[(N-methyl- pyrrolidin-2(R)-yl)methyl]indole. Macor, John E.; Chenard, Bert L.; Post, Ronald J. (Department of Medicinal Chemistry, Pfizer Inc., Groton, CT, 06340, USA). J. Org. Chem., 59(24), 7496-8 (English) 1994. CODEN: JOCEAH. ISSN: 0022-3263. OTHER SOURCES: CASREACT 121:280497; CJACS-IMAGE; CJACS.

AB 5-Amino-3-(N-methylpyrrolidin-2R-ylmethyl)indole was synthesized in an overall of 39% in four steps on a large scale. Crucial to the success of this sequence was the use of a 2,5-dimethylpyrrole as the protecting group for the 5-aminoindole functionality. This protecting group was stable to (unreactive toward) ethylmagnesium bromide, a hindered acid chloride (CBZ-proline acid chloride), and lithium aluminum hydride, but easily removed in high yield using unique conditions (hydroxylamine hydrochloride/triethylamine/propanol/water/.DELTA.).

IT 151273-49-3P 158752-53-5P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)
(use of dimethylpyrrole as an amino-protecting group in an efficient synthesis of amino[(methylpyrrolidinyl)methyl]indole)

IT 143322-01-4P
RL: SPN (Synthetic preparation); PREP (Preparation)
(use of dimethylpyrrole as an amino-protecting group in an efficient synthesis of amino[(methylpyrrolidinyl)methyl]indole)

L7 ANSWER 17 OF 124 CAPLUS COPYRIGHT 1996 ACS
1994:631280 Document No. 121:231280 Non-decarboxylative 1,3-dipolar cycloadditions of imines of .alpha.-amino acids as a route to proline derivatives. Aly, Moustafa F.; Younes, Mansour I.; Metwally, Saoud A. M. (Fac. Sci., Assiut Univ., Qena, Egypt). Tetrahedron, 50(10), 3159-68 (English) 1994. CODEN: TETRAB. ISSN: 0040-4020. OTHER SOURCES: CASREACT 121:231280.
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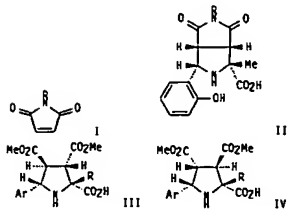

AB The 1,3-dipolar cycloaddn. reaction of alanine with salicylaldehyde and N-substituted maleimides I (R = Me, Ph) gave stereospecific cycloadducts II. The 1,3-dipolar cycloaddn. reaction of .alpha.-amino acids with aryl aldehydes in the presence of di-Me fumarate gave isomeric cycloadducts III (Ar = 2-hydroxyphenyl, R1 = Me, H, CH2CHMe2, CH2CH2SMe, CH2Ph, indol-3-ylmethyl; Ar Ph, 2-methoxyphenyl, 2,4-dimethoxyphenyl, R1 = Me) and IV (Ar and R1 = same). The relatively low yield in the case of di-Me fumarate is presumably due to the steric interaction between the dipolarophile and the substituents at both ends of the dipole.
IT 158134-75-9P 158249-37-7P
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of)

L7 ANSWER 18 OF 124 CAPLUS COPYRIGHT 1996 ACS
1994:574790 Document No. 121:174790 Antifungal substances produced by Chaetomium globosum. Asaeiya, Yoshimiki; Kondo, Akihiro; Hirano, Kazuya; Hirukawa, Toshihumi; Kato, Tadahiro (Fac. Hortic., Chiba Univ., Matsudo, 271, Japan). Chiba Daigaku Engeigakubu Gakujutsu Hokoku, 48, 13-18 (Japanese) 1994. CODEN: CDEGAF. ISSN: 0069-3227.
AB Antifungal substances were extd. from culture filtrate of the most antagonistic isolate identified as Chaetomium globosum. Two active substances were obtained by using silica gel column chromatog. and high performance liq. chromatog. By analyzing with mass spectrometer (EIMS, HR-MS), 1H-NMR and 13C-NMR, the major substance was identified as Chaetoglobosin A, one of the toxic metabolites produced by C. globosum and C. chochliodes. Another substance was assumed to have similar structure with Chaetoglobosin A. The major substance completely inhibited the spore germination of V. dahliae at 32 .mu.g/mL. It was also active against V. albo-atrum and Rhizoctonia solani, but not against Fusarium oxysporum, F. solani and Pythium aphanidermatum.
IT 50335-03-0, Chaetoglobosin A
RL: BAC (Biological activity or effector, except adverse); BIOL (Biological study)
(from Chaetomium globosum, antifungal activity of, against Verticillium and Rhizoctonia)

L7 ANSWER 19 OF 124 CAPLUS COPYRIGHT 1996 ACS
1994:553524 Document No. 121:153524 A novel mycotoxin: the chaetoglobosin N from infested maize by Phomopsis leptostromiformis. II. Structure elucidation by 1H and 13C NMR. Convert, O.; Jellal, A.; Correia, I.; Dardoize, F.; Menguy, L.; Cherton, J. C. (Lab. Chim. Organ. Struct., Univ. Pierre et Marie Curie, Paris, 75005, Fr.). Analusis, 22(4), 217-21 (English) 1994. CODEN: ANLSCY. ISSN: 0365-4877.
AB From culture on maize of the strain MRC 2654 of P. leptostromiformis, two fungal metabolites, unusual to this fungus, have been isolated in the methanolic ext. 1H and 13C NMR spectra allowed the establishment for these mols. some partial structures contg. an indole unit and several condensed cycles. On the basis of these NMR results, the compd. F = 185.degree. is identified to the term M of the chaetoglobosin series and the more polar compd., F = 205.degree., named chaetoglobosin N, appears to be a new term in this series.
IT 119212-28-1, Chaetoglobosin M
RL: BIOL (Biological study)
(from Phomopsis leptostromiformis-infected corn)
IT 156980-59-5, Chaetoglobosin N
RL: BIOL (Biological study)
(from Phomopsis leptostromiformis-infected corn, structure of)

L7 ANSWER 20 OF 124 CAPLUS COPYRIGHT 1996 ACS
1994:501581 Document No. 121:101581 Unexpected production of chaetoglobosins from maize incubated by Phomopsis leptostromiformis. I. Isolation and optimization of the production in liquid media by LC monitoring. Cherton, J. C.; Jellal, A.; Lhommet, G.; Loutelier, C.; Dardoize, F.; Lacoste, L.; Subileau, C. (Dep. Chim., Univ. Versailles Saint-Quentin Yvelines, Versailles, 78001, Fr.). Analusis, 22(4), 210-16 (English) 1994. CODEN: ANLSCY. ISSN: 0365-4877.
AB Attempts to obtain the toxin phomopsin A, usually isolated from P. leptostromiformis fungus, failed when infesting maize with strain MRC 2654 of this fungus. However, taking into account the acute toxicity for rats of the crude methanol ext., mycotoxins less polar than phomopsins were searched for by checking other sepn. procedures. Preparative silica TLC entailed the localization of the toxicity in the fraction sol. in iso-Pr ether. Preparative HPLC on silica allowed the purifn. of 2 toxins shown to belong to the chaetoglobosin series. A LC method for direct monitoring of the prodn. of these toxins in liq. media resulted in a first optimization of the culture conditions. It appeared that the yields of these toxins can be increased approx. 4-fold by reducing the culture of P. leptostromiformis in darkness from 28 to 10 days.
IT 156980-59-5, Chaetoglobosin N
RL: FORM (Formation, nonpreparative)
(formation of, by Phomopsis leptostromiformis, prodn. optimization and sepn. of, in liq. media by liq. chromatog. monitoring in relation to)
IT 119212-28-1, Chaetoglobosin M
RL: BIOL (Biological study)
(prodn. optimization and sepn. of, in liq. media by liq. chromatog. monitoring)

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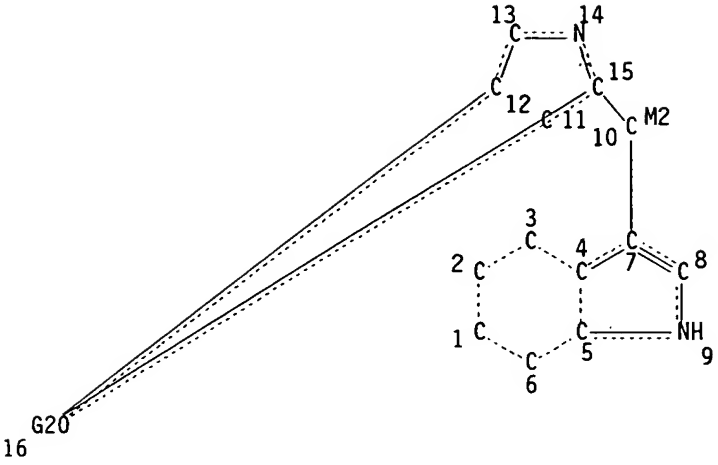
L3 STR



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GRAPH ATTRIBUTES:
RING(S) ARE ISOLATED OR EMBEDDED
NUMBER OF NODES IS 16

STEREO ATTRIBUTES: NONE
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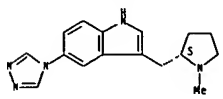
RN 171550-16-6 REGISTRY
CN INDEX NAME NOT YET ASSIGNED
FS STEREOSEARCH
MF C16 H19 N5 . x H2 O4 S
SR CA
LC STN Files: CAPLUS

CM 1

CRN 171550-15-5
CMF C16 H19 N5
CDES 1:S

Absolute stereochemistry.



CM 2

CRN 7664-93-9
CMF H2 O4 S

1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

L4 ANSWER 5 OF 756 REGISTRY COPYRIGHT 1996 ACS
RN 171182-32-4 REGISTRY
CN 1H-Indole, 3-(2-pyrrolidinylmethyl)-5-(4H-1,2,4-triazol-4-yl)-, (R)- (9CI) (CA INDEX NAME)
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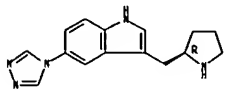
SR CA
LC STN Files: CA, CAPLUS, CAPREVIEWS
DES 1:R

Absolute stereochemistry.



1 REFERENCES IN FILE CAPREVIEWS
1 REFERENCES IN FILE CA (1967 TO DATE)
1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

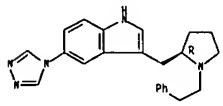
REFERENCE 1: 124:8823

L4 ANSWER 10 OF 756 REGISTRY COPYRIGHT 1996 ACS
RN 171182-27-7 REGISTRY
CN 1H-Indole, 3-[[1-(2-phenylethyl)-2-pyrrolidinyl]methyl]-5-(4H-1,2,4-triazol-4-yl)-, (R)-, ethanedioate (2:5) (9CI) (CA INDEX NAME)
FS STEREOSEARCH
MF C23 H25 N5 . 5/2 C2 H2 O4
SR CA
LC STN Files: CA, CAPLUS, CAPREVIEWS

CM 1

CRN 171182-26-6
CMF C23 H25 N5
CDES 1:R

Absolute stereochemistry.



CM 2

CRN 144-62-7
CMF C2 H2 O4

1 REFERENCES IN FILE CAPREVIEWS
1 REFERENCES IN FILE CA (1967 TO DATE)
1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

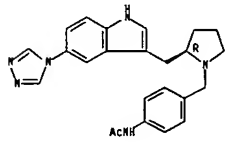
REFERENCE 1: 124:8823

L4 ANSWER 14 OF 756 REGISTRY COPYRIGHT 1996 ACS
RN 171182-23-3 REGISTRY
CN Acetamide, N-[4-[[2-[[5-(4H-1,2,4-triazol-4-yl)-1H-indol-3-yl]methyl]-1-pyrrolidinyl]methyl]phenyl]-, (R)-, ethanedioate (1:1) (9CI) (CA INDEX NAME)
FS STEREOSEARCH
MF C24 H26 N6 O . C2 H2 O4
SR CA
LC STN Files: CA, CAPLUS, CAPREVIEWS

CM 1

CRN 171182-22-2
CMF C24 H26 N6 O
CDES 1:R

Absolute stereochemistry.



CM 2

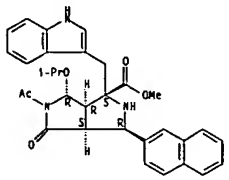
CRN 144-62-7
CMF C2 H2 O4

1 REFERENCES IN FILE CAPREVIEWS
1 REFERENCES IN FILE CA (1967 TO DATE)
1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 124:8823

L4 ANSWER 18 OF 756 REGISTRY COPYRIGHT 1996 ACS
RN 170027-95-9 REGISTRY
CN Pyrrolo[3,4-c]pyrrole-1-carboxylic acid, 5-acetyloctahydro-1-(1H-indol-3-ylmethyl)-6-(1-methylethoxy)-3-(2-naphthalenyl)-4-oxo-, methyl ester, [1S-(1.alpha.,3.alpha.,3a.beta.,6.beta.,6a.beta.)]- (9CI) (CA INDEX NAME)
FS STEREOSEARCH
MF C32 H33 N3 O5
SR CA
LC STN Files: CA, CAPLUS
DES *

Absolute stereochemistry.

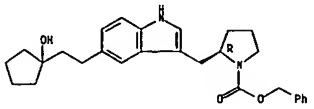


1 REFERENCES IN FILE CA (1967 TO DATE)
1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 123:313894

L4 ANSWER 28 OF 756 REGISTRY COPYRIGHT 1996 ACS
RN 167303-56-2 REGISTRY
CN 1-Pyrrolidinecarboxylic acid, 2-[[5-[2-(1-hydroxycyclopentyl)ethyl]-1H-indol-3-yl]methyl]-, phenylmethyl ester, (R)- (9CI) (CA INDEX NAME)
FS STEREOSEARCH
MF C28 H34 N2 O3
SR CA
LC STN Files: CA, CAPLUS
DES 1:R

Absolute stereochemistry.

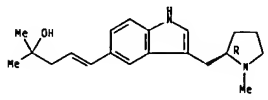


1 REFERENCES IN FILE CA (1967 TO DATE)
1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 123:169499

L4 ANSWER 44 OF 756 REGISTRY COPYRIGHT 1996 ACS
RN 167303-39-1 REGISTRY
CN 4-Penten-2-ol, 2-methyl-5-[3-[(1-methyl-2-pyrrolidinyl)methyl]-1H-indol-5-yl]-, (R)- (9CI) (CA INDEX NAME)
FS STEREOSEARCH
MF C20 H28 N2 O
SR CA
LC STN Files: CA, CAPLUS
DES 1:R

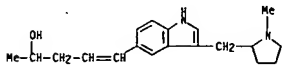
Absolute stereochemistry.
Double bond geometry unknown.



1 REFERENCES IN FILE CA (1967 TO DATE)
1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 123:169499

L4 ANSWER 48 OF 756 REGISTRY COPYRIGHT 1996 ACS
RN 167303-35-7 REGISTRY
CN 4-Penten-2-ol, 5-[3-[(1-methyl-2-pyrrolidinyl)methyl]-1H-indol-5-yl]- (9CI) (CA INDEX NAME)
FS 3D CONCORD
MF C19 H26 N2 O
SR CA
LC STN Files: CA, CAPLUS

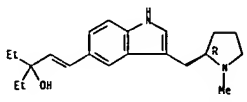


1 REFERENCES IN FILE CA (1967 TO DATE)
1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 123:169499

L4 ANSWER 54 OF 756 REGISTRY COPYRIGHT 1996 ACS
RN 167303-29-9 REGISTRY
CN 1-Penten-3-ol, 3-ethyl-1-[3-[(1-methyl-2-pyrrolidinyl)methyl]-1H-indol-5-yl]-, (R)- (9CI) (CA INDEX NAME)
FS STEREOSEARCH
MF C21 H30 N2 O
SR CA
LC STN Files: CA, CAPLUS
DES 1:R

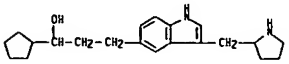
Absolute stereochemistry.
Double bond geometry unknown.



1 REFERENCES IN FILE CA (1967 TO DATE)
1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 123:169499

L4 ANSWER 68 OF 756 REGISTRY COPYRIGHT 1996 ACS
RN 167303-14-2 REGISTRY
CN 1H-Indole-5-propanol, .alpha.-cyclopentyl-3-(2-pyrrolidinylmethyl)- (9CI) (CA INDEX NAME)
FS 3D CONCORD
MF C21 H30 N2 O
SR CA
LC STN Files: CA, CAPLUS

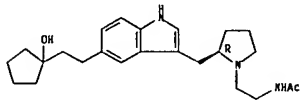


1 REFERENCES IN FILE CA (1967 TO DATE)
1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 123:169499

L4 ANSWER 73 OF 756 REGISTRY COPYRIGHT 1996 ACS
RN 167303-09-5 REGISTRY
CN Acetamide, N-[2-[2-[[5-[2-(1-hydroxycyclopentyl)ethyl]-1H-indol-3-yl]methyl]-1-pyrrolidinyl]ethyl]-, (R)- (9CI) (CA INDEX NAME)
FS STEREOSEARCH
MF C24 H35 N3 O2
SR CA
LC STN Files: CA, CAPLUS
DES 1:R

Absolute stereochemistry.

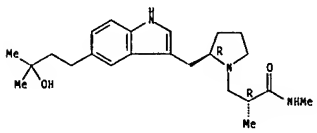


1 REFERENCES IN FILE CA (1967 TO DATE)
1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 123:169499

L4 ANSWER 89 OF 756 REGISTRY COPYRIGHT 1996 ACS
RN 167302-93-4 REGISTRY
CN 1-Pyrrolidinepropanamide, 2-[[5-(3-hydroxy-3-methylbutyl)-1H-indol-3-yl]methyl]-N,.alpha.-dimethyl-, [R-(R*,R*)]- (9CI) (CA INDEX NAME)
FS STEREOSEARCH
MF C23 H35 N3 O2
SR CA
LC STN Files: CA, CAPLUS
DES 1:R2:R*,R*

Absolute stereochemistry.

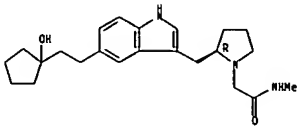


1 REFERENCES IN FILE CA (1967 TO DATE)
1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 123:169499

L4 ANSWER 101 OF 756 REGISTRY COPYRIGHT 1996 ACS
RN 167302-74-1 REGISTRY
CN 1-Pyrrolidineacetamide, 2-[[5-[2-(1-hydroxycyclopentyl)ethyl]-1H-indol-3-yl]methyl]-N-methyl-, (R)- (9CI) (CA INDEX NAME)
FS STEREOSEARCH
MF C23 H33 N3 O2
SR CA
LC STN Files: CA, CAPLUS
DES 1:R

Absolute stereochemistry.

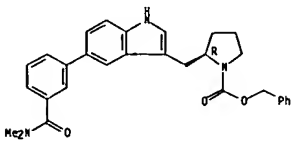


1 REFERENCES IN FILE CA (1967 TO DATE)
1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 123:169499

L4 ANSWER 254 OF 756 REGISTRY COPYRIGHT 1996 ACS
RN 153435-54-2 REGISTRY
CN 1-Pyrrolidinecarboxylic acid, 2-[[5-[3-[(dimethylamino)carbonyl]phenyl]-1H-indol-3-yl]methyl]-, phenylmethyl ester, (R)- (9CI) (CA INDEX NAME)
FS STEREOSEARCH
MF C30 H31 N3 O3
SR CA
LC STN Files: CA, CAPLUS
DES 1:R

Absolute stereochemistry.

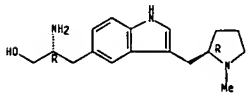


1 REFERENCES IN FILE CA (1967 TO DATE)
1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 120:217271

L4 ANSWER 330 OF 756 REGISTRY COPYRIGHT 1996 ACS
RN 152305-25-4 REGISTRY
CN 1H-Indole-5-propanol, .beta.-amino-3-[(1-methyl-2-pyrrolidinyl)methyl]-, [R-(R*,R*)]- (9CI) (CA INDEX NAME)
FS STEREOSEARCH
MF C17 H25 N3 O
SR CA
LC STN Files: CA, CAPLUS
DES 1:R2:R*,R*

Absolute stereochemistry.

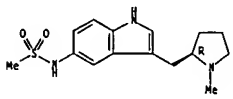


1 REFERENCES IN FILE CA (1967 TO DATE)
1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 120:106761

L4 ANSWER 458 OF 756 REGISTRY COPYRIGHT 1996 ACS
RN 143322-03-6 REGISTRY
CN Methanesulfonamide, N-[3-[(1-methyl-2-pyrrolidinyl)methyl]-1H-indol-5-yl]-, (R)- (9CI) (CA INDEX NAME)
FS STEREOSEARCH
MF C15 H21 N3 O2 S
SR CA
LC STN Files: CA, CAPLUS
DES 1:R

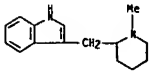
Absolute stereochemistry.



1 REFERENCES IN FILE CA (1967 TO DATE)
1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 117:171215

L4 ANSWER 529 OF 756 REGISTRY COPYRIGHT 1996 ACS
RN 111141-39-0 REGISTRY
CN Indole, 3-[(1-methyl-2-piperidyl)methyl]-, hydrochloride (6CI) (CA INDEX NAME)
MF C15 H20 N2 . Cl H
SR CAOLD
LC STN Files: BEILSTEIN*, CAOLD
(*File contains numerically searchable property data)
CRN (101832-07-9)

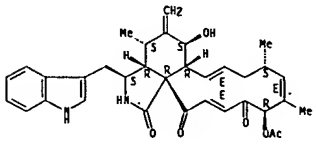


●HCl

1 REFERENCES IN FILE CAOLD (PRIOR TO 1967)

L4 ANSWER 578 OF 756 REGISTRY COPYRIGHT 1996 ACS
RN 80375-19-5 REGISTRY
CN [13]Cytochalasa-6(12),13,17,21-tetraene-1,20,23-trione, 19-(acetyloxy)-7-hydroxy-10-(1H-indol-3-yl)-16,18-dimethyl-, (7S,13E,16S,17E,19R,21E)- (9CI) (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN 1H-Cyclotridec[d]isoindole, [13]cytochalasa-6(12),13,17,21-tetraene-1,20,23-trione deriv.
OTHER NAMES:
CN 19-O-Acetylchaetoglobosin D
CN Chaetoglobosin D 19-acetate
FS STEREOSEARCH
MF C34 H38 N2 O6
LC STN Files: CA, CAPLUS, NAPRALERT
DES 4:7S,13E,16S,17E,19R,21E.(13)CYTOCHALASAN

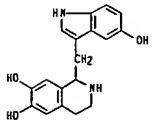
Absolute stereochemistry.
Double bond geometry as described by E or Z.



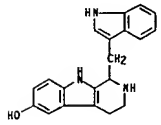
1 REFERENCES IN FILE CA (1967 TO DATE)
1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 96:31294

L4 ANSWER 600 OF 756 REGISTRY COPYRIGHT 1996 ACS
RN 70265-28-0 REGISTRY
CN 6,7-Isoquinolinediol, 1,2,3,4-tetrahydro-1-[(5-hydroxy-1H-indol-3-yl)methyl]- (9CI) (CA INDEX NAME)
FS 3D CONCORD
MF C18 H18 N2 O3
CI COM
LC STN Files: BEILSTEIN*
(*File contains numerically searchable property data)



L4 ANSWER 618 OF 756 REGISTRY COPYRIGHT 1996 ACS
RN 61326-52-1 REGISTRY
CN 1H-Pyrido[3,4-b]indol-6-ol, 2,3,4,9-tetrahydro-1-(1H-indol-3-ylmethyl)- (9CI) (CA INDEX NAME)
FS 3D CONCORD
MF C20 H19 N3 O
CI COM
LC STN Files: BEILSTEIN*, CA, CAPLUS, IFICDB, IFIPAT, IFIUDB, USPATFULL
(*File contains numerically searchable property data)

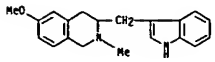


2 REFERENCES IN FILE CA (1967 TO DATE)
2 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 90:38902

REFERENCE 2: 86:29789

L4 ANSWER 723 OF 756 REGISTRY COPYRIGHT 1996 ACS
RN 16957-67-8 REGISTRY
CN Isoquinoline, 1,2,3,4-tetrahydro-3-(indol-3-ylmethyl)-6-methoxy-2-methyl- (8CI) (CA INDEX NAME)
FS 3D CONCORD
MF C20 H22 N2 O
LC STN Files: BEILSTEIN*, CA, CAPLUS
(*File contains numerically searchable property data)

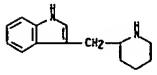


2 REFERENCES IN FILE CA (1967 TO DATE)
2 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 71:124750

REFERENCE 2: 69:67588

L4 ANSWER 755 OF 756 REGISTRY COPYRIGHT 1996 ACS
RN 5275-05-8 REGISTRY
CN 1H-Indole, 3-(2-piperidinylmethyl)- (9CI) (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN Indole, 3-(2-piperidylmethyl)- (6CI, 7CI, 8CI)
OTHER NAMES:
CN 3-(2-Piperidylmethyl)indole
FS 3D CONCORD
MF C14 H18 N2
CI COM
LC STN Files: BEILSTEIN*, CA, CAOLD, CAPLUS, CJACS, RTECS*
(*File contains numerically searchable property data)



5 REFERENCES IN FILE CA (1967 TO DATE)
5 REFERENCES IN FILE CAPLUS (1967 TO DATE)
5 REFERENCES IN FILE CAOLD (PRIOR TO 1967)

REFERENCE 1: 117:171215

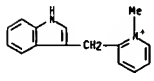
REFERENCE 2: 117:26178

REFERENCE 3: 98:160991

REFERENCE 4: 91:140663

REFERENCE 5: 77:126393

L4 ANSWER 756 OF 756 REGISTRY COPYRIGHT 1996 ACS
RN 5275-03-6 REGISTRY
CN Pyridinium, 2-(1H-indol-3-ylmethyl)-1-methyl-, iodide (9CI) (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN 2-(Indol-3-ylmethyl)-1-methylpyridinium iodide (6CI, 7CI)
CN Pyridinium, 2-(1indol-3-ylmethyl)-1-methyl-, iodide (8CI)
MF C15 H15 N2 . I
LC STN Files: BEILSTEIN*, CAOLD, TOXLIT
(*File contains numerically searchable property data)
CRN (17795-28-7)



●I-

2 REFERENCES IN FILE CAOLD (PRIOR TO 1967)

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FILE 'CAOLD' ENTERED AT 18:41:53 ON 07 JAN 96
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FILE COVERS 1957-1966
FILE LAST UPDATED:  30 OCT 91 (910803/ED)

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  numbers of terms.

=> s 14
L5          20 L4

=> d 1-20
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L5 ANSWER 1 OF 20 COPYRIGHT 1996 ACS
AN CA65:18640c
IT 10438-16-1 10438-17-2 10438-19-4 20165-95-1

L5 ANSWER 2 OF 20 COPYRIGHT 1996 ACS
AN CA65:16973a
DT P
IT 7670-46-4 7695-23-0 17971-17-4 99813-09-9

L5 ANSWER 3 OF 20 COPYRIGHT 1996 ACS
AN CA65:13714a
DT P
IT 7546-61-4 7546-63-6 16060-17-6

L5 ANSWER 4 OF 20 COPYRIGHT 1996 ACS
AN CA65:13713h
DT P
IT 7546-58-9 7546-59-0 7551-14-6 101811-43-2

L5 ANSWER 5 OF 20 COPYRIGHT 1996 ACS
AN CA65:13713f
DT P
IT 7551-08-8 14128-30-4

L5 ANSWER 6 OF 20 COPYRIGHT 1996 ACS
AN CA65:13713e
DT P
IT 7546-60-3 7551-09-9

L5 ANSWER 7 OF 20 COPYRIGHT 1996 ACS
AN CA64:17539b
IT 5697-98-3 5697-99-4

L5 ANSWER 8 OF 20 COPYRIGHT 1996 ACS
AN CA64:14161g
IT 3515-49-9 5275-03-6 5275-04-7 5275-05-8 5275-06-9
5275-07-0 5275-08-1 5275-09-2 5275-40-1 5275-41-2
5275-42-3 5275-43-4 5353-44-6 5353-45-7 5580-44-9
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L5 ANSWER 9 OF 20 COPYRIGHT 1996 ACS
AN CA61:13278a
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94801-80-6 95133-76-9 96977-54-7 97115-04-3

L5 ANSWER 10 OF 20 COPYRIGHT 1996 ACS
AN CA57:1657a
DT P
IT 5275-05-8 58383-32-7

L5 ANSWER 11 OF 20 COPYRIGHT 1996 ACS
AN CA55:11442f
DT P
IT 5275-05-8 92647-88-6 100168-19-2 102461-04-1

L5 ANSWER 12 OF 20 COPYRIGHT 1996 ACS
AN CA53:13146f
IT 110421-90-4

L5 ANSWER 13 OF 20 COPYRIGHT 1996 ACS
AN CA53:13146d
IT 103268-60-6 132887-26-4

L5 ANSWER 14 OF 20 COPYRIGHT 1996 ACS
AN CA53:6226f
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110179-78-7

L5 ANSWER 15 OF 20 COPYRIGHT 1996 ACS
AN CA53:3146e
IT 102173-76-2

L5 ANSWER 16 OF 20 COPYRIGHT 1996 ACS
AN CA52:5406f
IT 111141-39-0

L5 ANSWER 17 OF 20 COPYRIGHT 1996 ACS
AN CA52:5406e
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L5 ANSWER 18 OF 20 COPYRIGHT 1996 ACS
AN CA51:6702h
DT P
IT 5275-03-6 5580-44-9

L5 ANSWER 19 OF 20 COPYRIGHT 1996 ACS
AN CA51:6702g
DT P
IT 100880-55-5

L5 ANSWER 20 OF 20 COPYRIGHT 1996 ACS
AN CA51:6702f
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IT 102025-60-5 111529-88-5

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=> fil caplus
FILE 'CAPLUS' ENTERED AT 18:42:36 ON 07 JAN 96
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FILE COVERS 1967 - 7 Jan 1996  VOL 124 ISS 2
FILE LAST UPDATED: 6 Jan 1996  (960106/ED)

  To help control your online searching costs, consider using the
  HCAplus file when using the FSEARCH command or when conducting
  SmartSELECT searches with large numbers of terms.


=> s l4
L6          180 L4

=> d 1-40 cbib abs hitrn
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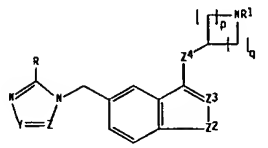
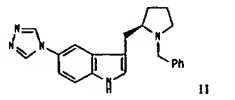
L6 ANSWER 1 OF 180 CAPLUS COPYRIGHT 1996 ACS
1995:987946 Preparation of [(triazolyl)indolyl]methylpyrrolidines as 5-HT1-like agonists.. Matassa, Victor Giulio; Sternfeld, Francine; Street, Leslie Joseph (Merck Sharp and Dohme Ltd., UK). PCT Int. Appl. WO 9521167 A1 950810, 22 pp. DESIGNATED STATES: W: AM, AT, AU, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, JP, KE, KG, KP, KR, KZ, LK, LR, LT, LU, LV, MD, MG, MN, MW, MX, NL, NO, NZ, PL, PT, RO, RU, SD, SE, SI, SK, TJ, TT, UA, US; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, DE, DK, ES, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG. (English). CODEN: PIXXD2. APPLICATION: WO 95-GB135 950124. PRIORITY: GB 94-2011 940202.
AB Title compds. (I; R = H, C1-6 alkyl), were prepd. Thus, 4'-(1,2,4-triazol-4-yl)phenylhydrazine and (2S)-N-tert-butoxycarbonyl-3-(pyrrolidin-2-yl)propanal were stirred in 4% aq. H2SO4 at room temp.-reflux to give 34% I (R = H), isolated as the oxalate. I showed pEC50 .gtoreq.5.0 in a test of their ability to mediate contraction of the saphenous vein of rabbits.
IT RN LIST MAY NOT BE COMPLETE: 154594-16-8 171550-13-3
171550-14-4 171550-15-5 171550-16-6
171752-92-4

L6 ANSWER 2 OF 180 CAPLUS COPYRIGHT 1996 ACS
1995:969448 Document No. 124:8823 Preparation of triazole derivatives as serotoninergic agonists. Matassa, Victor Giulio; Sternfeld, Francine; Street, Leslie Joseph (Merck Sharp and Dohme Ltd., UK). PCT Int. Appl. WO 9521166 A1 950810, 49 pp. DESIGNATED STATES: W: AM, AT, AU, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, JP, KE, KG, KP, KR, KZ, LK, LR, LT, LU, LV, MD, MG, MN, MW, MX, NL, NO, NZ, PL, PT, RO, RU, SD, SE, SI, SK, TJ, TT, UA, US; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, DE, DK, ES, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG. (English). CODEN: PIXXD2. APPLICATION: WO 95-GB134 950124. PRIORITY: GB 94-2016 940202.
GI



I



II

AB Title compds. [I; R = H, hydrocarbyl, heterocyclyl, etc.; R1 = cycloalkyl, alkoxyalkyl, aryl(alkyl), etc.; 1 of Y,Z = N and the other = (un)substituted CH; Z1 = bond, alkylene; Z2 = O, S, (alkyl)imino; Z3 = N, (alkyl-substituted)CH; Z4 = alkylene; p = 0 or 1; q = 1-4; p+q = 2-4], agonists of 5-HT1-like receptors, were prepd. Thus, (2R)-N-tert-butoxycarbonylpyrrolidine-2-propanal was cyclocondensed with 4-(1,2,4-triazol-4-yl)phenylhydrazine (prepn. each given) and the product condensed with PhCHO to give title compd. II. I had pEC50 of .gtoreq.5.0 for contraction of rabbit saphenous vein.
IT 171182-20-0P 171182-21-1P 171182-22-2P
171182-23-3P 171182-24-4P 171182-25-5P
171182-26-6P 171182-27-7P 171182-28-8P
171182-29-9P 171182-30-2P 171182-31-3P
RL: BAC (Biological activity or effector, except adverse); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

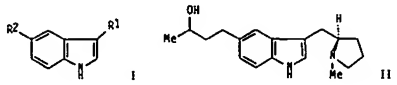
L6 ANSWER 2 OF 180 CAPLUS COPYRIGHT 1996 ACS (Continued)
(prepn. of triazole derivs. as serotoninergic agonists)
IT 171182-32-4P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)
(prepn. of triazole derivs. as serotoninergic agonists)

L6 ANSWER 3 OF 180 CAPLUS COPYRIGHT 1996 ACS
1995:933846 Document No. 124:688 The in vivo pharmacological profile of a 5-HT1 receptor agonist, CP-122,288, a selective inhibitor of neurogenic inflammation. Gupta, P.; Brown, D.; Butler, P.; Ellis, P.; Grayson, K. L.; Land, G. C.; Macor, J. E.; Robson, S. F.; Wythes, M. J.; Shepperson, N. B. (Departments of Discovery Biology and Discovery Chemistry, Pfizer Central Research, Sandwich, Kent, CT13 9NJ, UK). Br. J. Pharmacol., 116(5), 2385-90 (English) 1995. CODEN: BJPCBM. ISSN: 0007-1188.
AB The aim of the present study was to investigate the in vivo pharmacol. profile of CP-122,288, an indole-deriv. with a conformationally restricted N-methylpyrrolidinyl basic side chain in the C-3 position. This C-3 substituent structurally differentiates CP-122,288 from the 5-HT1D receptor agonist sumatriptan, which possesses an N,N-dimethylaminoethyl group. When administered prior to elec. stimulation of the trigeminal ganglion, CP-122,288 (0.3-300 ng kg-1, i.v.) produced a dose-related inhibition of plasma protein extravasation in rat dura mater (min. ED, MED, 3 ng kg-1 i.v., P < 0.05; maximal inhibition of plasma extravasation at 30 ng kg-1 i.v., P < 0.01). Sumatriptan produced a similar inhibition of plasma leakage in the dura, but at much higher dose levels (MED, 100 .mu.g kg-1 i.v., P < 0.05). Thus, CP-122,288 is of the order of 104 fold more potent than sumatriptan. At all doses tested, CP-122,288 did not inhibit plasma protein extravasation measured in extracranial tissues such as the lower lip, eyelid, and conjunctiva. In a sep. series of studies in the anesthetized rat, CP-122,288 (0.003-3 .mu.g kg-1 i.v.) produced no change in either heart rate or mean arterial blood pressure, thus demonstrating that doses of CP-122,288 which inhibit plasma protein leakage in rat dura, are devoid of hemodynamic effects. Following a 5 min period of elec. stimulation of the trigeminal ganglion, a 20 min period of sustained neurogenically-driven plasma extravasation, occurring in the absence of elec. stimulation, was initiated. By administration of the compd. 5 min after completing the phase of elec. stimulation, this protocol permitted the evaluation of the activity of CP-122,288 on the ongoing and established inflammatory event. CP-122,288 (30 and 300 ng kg-1, i.v. P <0.01 and P <0.05, resp.) produced a complete inhibition of plasma protein leakage which was consistent with its effects when administered prior to trigeminal ganglion stimulation. In the anesthetized dog, CP-122,288 and sumatriptan, at 1-300 .mu.g kg-1, i.v., produced a dose-dependent redn. in carotid arterial blood flow and coronary arterial diam. These data demonstrate that sumatriptan inhibits neurogenic inflammation in the rat (MED, 100 .mu.g kg-1, i.v.) and produces vasoconstriction in the dog, over a similar dose-range. Interestingly, doses of CP 122,288 that inhibit neurogenic inflammation in rat dura mater (0.3-300 ng kg-1) were demonstrated to be devoid of vasoconstrictor activity in either the carotid or coronary vascular beds of dog. These data demonstrate that in the rat, CP-122,288 is a highly potent and selective inhibitor of neurogenic inflammation in intracranial tissues, at doses which are devoid of vasoconstrictor activity in dog. Potentially, CP-122,288 may be of use for the acute treatment of migraine, without the risk of cardiovascular side-effects.
IT 143321-74-8, CP-122288
RL: ADV (Adverse effect, including toxicity); BAC (Biological activity or effector, except adverse); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

L6 ANSWER 3 OF 180 CAPLUS COPYRIGHT 1996 ACS (Continued)
(CP-122,288 pharmacol. profile as selective inhibitor of neurogenic inflammation in relation to migraine treatment)

L6 ANSWER 4 OF 180 CAPLUS COPYRIGHT 1996 ACS
1995:772570 Document No. 123:169499 Indole derivatives as 5-HT1-like agonists for use in migraine. Wythes, Martin James (Pfizer Ltd., UK; Pfizer Inc.; Pfizer Research and Development Company, N.V./S.A.). PCT Int. Appl. WO 9424127 A1 941027, 124 pp. DESIGNATED STATES: W: AU, BR, CA, CN, CZ, FI, HU, JP, KR, NO, NZ, PL, RU, US; RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE. (English). CODEN: PIXXD2. APPLICATION: WO 94-EP1121 940411. PRIORITY: GB 93-8360 930422; GB 93-24433 931127.

GI



AB The title compds., 3-(pyrrolidinylmethyl)indoles and 3-(piperidinylmethyl)indoles I [R1 = (2-pyrrolidinyl)methyl, 3-pyrrolidinyl, 4-piperidinyl, (3-piperidinyl)methyl; R2 = alkyl, oxoalkyl, etc.] were disclosed as selective 5-HT1-like agonists useful in the treatment of migraine, cluster headache, chronic paroxysmal hemicrania and headache assocd. with vascular disorders. A specifically claimed example compd. is 5-(3-hydroxybutyl)-3-[(R)-(1-methyl-2-pyrrolidinyl)methyl]-1-H-indole (II).

IT 143322-57-0
RL: RCT (Reactant)
(prepn. of (pyrrolidinylmethyl)indoles 5-HT1-like agonists)

IT 143322-46-7P 153435-71-3P 153435-73-5P
153525-35-0P 153525-50-9P 153525-51-0P
167303-50-6P 167303-51-7P 167303-54-0P
167303-55-1P 167303-56-2P 167303-63-1P
167303-64-2P 167303-66-4P 167303-67-5P
167303-71-1P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)
(prepn. of (pyrrolidinylmethyl)indoles 5-HT1-like agonists)

IT 167302-44-5P 167302-45-6P 167302-46-7P
167302-47-8P 167302-48-9P 167302-49-0P
167302-50-3P 167302-51-4P 167302-52-5P
167302-53-6P 167302-54-7P 167302-55-8P
167302-56-9P 167302-62-7P 167302-63-8P
167302-64-9P 167302-65-0P 167302-66-1P
167302-71-8P 167302-72-9P 167302-73-0P
167302-74-1P 167302-75-2P 167302-76-3P
167302-77-4P 167302-78-5P 167302-79-6P
167302-80-9P 167302-81-0P 167302-82-1P
167302-83-2P 167302-84-3P 167302-92-3P
167302-93-4P 167302-94-5P 167302-95-6P
167302-96-7P 167302-97-8P 167302-98-9P
167302-99-0P 167303-00-6P 167303-01-7P

L6 ANSWER 4 OF 180 CAPLUS COPYRIGHT 1996 ACS (Continued)
167303-02-8P 167303-03-9P 167303-04-0P
167303-05-1P 167303-06-2P 167303-07-3P
167303-08-4P 167303-09-5P 167303-10-8P
167303-11-9P 167303-12-0P 167303-13-1P
167303-14-2P 167303-15-3P 167303-16-4P
167303-17-5P 167303-18-6P 167303-19-7P
167303-20-0P 167303-21-1P 167303-23-3P
167303-24-4P 167303-25-5P 167303-26-6P
167303-27-7P 167303-28-8P 167303-29-9P
167303-30-2P 167303-31-3P 167303-32-4P
167303-33-5P 167303-34-6P 167303-35-7P
167303-36-8P 167303-37-9P 167303-38-0P
167303-39-1P 167303-40-4P 167303-41-5P
167303-42-6P 167303-43-7P 167303-44-8P
167303-45-9P 167303-46-0P 167303-47-1P
167303-48-2P 167303-49-3P 167303-53-9P
167303-57-3P
RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of (pyrrolidinylmethyl)indoles 5-HT1-like agonists)

L6 ANSWER 5 OF 180 CAPLUS COPYRIGHT 1996 ACS
1995:685346 Document No. 123:313894 Z+Y-ZH compounds as potential 1,3-dipoles. Part 44. Asymmetric 1,3-dipolar cycloaddition reactions of imines and chiral cyclic dipolarophiles. Cooper, Daniel M.; Grigg, Ronald; Hargreaves, Simon; Kennewell, Peter; Redpath, James (Sch. Chem., Leeds Univ., Leeds, LS2 9JT, UK). Tetrahedron, 51(28), 7791-808 (English) 1995. CODEN: TETRAB. ISSN: 0040-4020.

AB Metallo-1,3-dipoles generated in situ from both aryl and aliph. imines of .alpha.-amino esters by the action of silver salts and tertiary amines undergo cycloaddn. at room temp. to give (menthyl)furo[3,4-c]pyrrolecarboxylates pyrrolopyrrolecarboxyates. .pi.-Interaction between the dipolarophile carbonyl group and the aryl group in the aryl imines is not required for good induction. The stronger the base the faster the cycloaddn. with 2-t-butyl-1,1,3,3-tetramethylguanidine > DBU > NEt3. X-ray crystal structures of representative cycloadducts established the abs. configuration of the pyrrolidine stereocenters.

IT 170027-89-1P 170027-95-9P
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of)

L6 ANSWER 6 OF 180 CAPLUS COPYRIGHT 1996 ACS
1995:611905 Document No. 123:41025 Opportunities and limitations of modern TLC/HPTLC in the quality control of L-tryptophan. Jork, Hellmut; Ganz, Jutta (Department Pharmacy und Biological Chemistry, University Saarland, Saarbruecken, 66041, Germany). L-Tryptophan: Curr. Prospects Med. Drug Saf., 338-50. Editor(s): Kochen, Walter; Steinhart, Hans. de Gruyter: Berlin, Germany. (English) 1994. CODEN: 61JRA9.
AB Ascending, one-dimensional development of chromatograms was carried out on Chiralplates (10 x 20 cm) in a trough chamber with chamber satn. The mobile phase was acetonitrile-methanol-water (40-10-10, vol./vol./v). The chromatog. was completed after 10 min (distance run 6 cm). The zones were stained by dipping (1 s) in a ninhydrin soln. and heating to 110.degree. for 5 min. Bluish-red zones were produced on colorless backgrounds for L-tryptophan, D-tryptophan, and 1,1'-ethylidene-bis(L-tryptophan). Only the two diastereomers 3-carboxy-1-(3-indolylmethyl)-1,2,3,4-tetrahydro-.beta.-carboline were stained ochre yellow. The selectivity of thin-layer chromatog. sepn. is so great that L-and D-tryptophan and 1,1'-ethylidene-bis(L-tryptophan) can be sepd. excellently. Nor is there any difficulty in sepg. L-tryptophan, 1,1'-ethylidene-bis(L-tryptophan), 3-carboxy-1,2,3,4-tetrahydro-.beta.-carboline and 3-carboxy-1-methyl-1,2,3,4-tetrahydro-.beta.-carboline.
IT 164068-18-2 164203-07-0
RL: ANT (Analyte); ANST (Analytical study)
(opportunities and limitations of modern TLC/HPTLC in the quality control of L-tryptophan)

L6 ANSWER 7 OF 180 CAPLUS COPYRIGHT 1996 ACS
1995:575044 Document No. 122:309995 Differentiating Penicillium species by detection of indole metabolites using a filter paper method. Lund, F. (Department of Biotechnology, Technical University of Denmark, Lyngby, Den.). Lett. Appl. Microbiol., 20(4), 228-31 (English) 1995. CODEN: LAMIE7. ISSN: 0266-8254.
AB The indole secondary metabolites chaetoglobosin C, cyclopiazonic acid, isofumigaclavine A and rugulovasine A and B produced by several Penicillium species growing on Czapek yeast autolyzate agar were detected directly in the culture using filter paper wetted with Ehrlich reagent dissolved in ethanol. The filter paper was placed on the mycelial side of an agar plug and the metabolites were visualized as a violet zone on the paper within 10 min. It was shown that the combined characters of the violet reaction on filter paper and the ability to grow on creatine sucrose agar occurred in 5 out of 16 species of Penicillium exmd. A few addnl. simple morphol. and physiol. criteria were then sufficient for identification of P. camemberti, P. commune, P. discolor, P. expansum and P. roueforti var. rouqueforti.
IT 50645-76-6, Chaetoglobosin C
RL: ANT (Analyte); ANST (Analytical study)
(Differentiating Penicillium species by detection of indole metabolites using a filter paper method)

L6 ANSWER 8 OF 180 CAPLUS COPYRIGHT 1996 ACS
1995:549880 Document No. 122:306133 Effect of a 5-HT1 receptor agonist, CP-122,288, on edema formation induced by stimulation of the rat saphenous nerve. Kajekar, Radhika; Gupta, Paul; Shepperson, Nicholas B.; Brain, Susan D. (Vascular Biology Research Centre, King's College, London, SW3 6LX, UK). Br. J. Pharmacol., 115(1), 1-2 (English) 1995. CODEN: BJPCBM. ISSN: 0007-1188.
AB Neurogenic edema formation in the rat hind paw skin induced by elec. stimulation of the saphenous nerve and measured by extravasation of [125I]-albumin, was inhibited by the 5-HT1B receptor agonist, CP-93,129, and the novel tryptamine analog, CP-122,288. Significant inhibition of up to 66% of control was obsd. with CP-122,288 (2 .times. 10-14 - 2 .times. 10-7 mol kg-1) and CP-93,129 (5 .times. 10-7-5 .times. 10-6 mol kg-1), with the min. ED for CP-122,288 being about 107 fold less than that for GP-93,129. Edema formation induced by the intradermal administration of exogenous mediators (substance P and histamine) in rat dorsal skin was not inhibited by CP-122,288 (2 .times. 10-10 mol kg-1). These results suggest that CP-122,288 is a potent inhibitor of neurogenic inflammation in rat skin and that the effect may be due to a prejunctional inhibition of neuropeptide release.
IT 143321-74-8, CP-122288
RL: BAC (Biological activity or effector, except adverse); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(neurogenic edema inhibition by 5-HT1 receptor agonist CP-122288)

L6 ANSWER 9 OF 180 CAPLUS COPYRIGHT 1996 ACS
1995:521096 Document No. 122:310000 High-performance liquid chromatography comparison of supercritical-fluid extraction and solvent extraction of microbial fermentation products. Cocks, Simon; Wrigley, Stephen K.; Chicarelli-Robinson, M. Ines; Smith, Roger M. (Xenova Ltd, 240 Bath Road, Slough Berkshire, SL1 4EQ, UK). J. Chromatogr., A, 697(1 + 2), 115-22 (English) 1995. CODEN: JCRAEY.
AB The use of supercrit. fluids for the extn. of biol. active compds. from the biomass of microbial ferms. has been compared with extn. using the org. solvents methanol and dichloromethane. Compds. representing a range of structural types were selected for investigation. All the exts. obtained were exmd. by reversed-phase HPLC. The extractability of metabolites using unmodified and methanol-modified supercrit.-fluid carbon dioxide was exmd. in particular detail for six microbial metabolites: chaetoglobosin A, mycolutein, luteoreticulin, 7,8-dihydro-7,8-epoxy-1-hydroxy-3-hydroxymethylxanthone-8-carboxylic acid Me ester, sydowinin B and elatophylin. The extn. strength of supercrit.-fluid carbon dioxide alone appeared to be lower than that of dichloromethane. All the components of interest that were extractable with dichloromethane and methanol were also extractable with methanol-modified carbon dioxide.
IT 50335-03-0P, Chaetoglobosin A
RL: PUR (Purification or recovery); PREP (Preparation)
(HPLC comparison of supercrit.-fluid vs. solvent extn. of microbial ferm. products)

L6 ANSWER 10 OF 180 CAPLUS COPYRIGHT 1996 ACS
1995:517652 Document No. 123:33479 Synthesis of Aristotelia-type alkaloids. Part XV. Total synthesis of (+)-hobartinol. Dobler, Markus; Anderson, James C.; Juch, Mathias; Borschberg, Hans-Juerg (Lab. Org. Chem., Eidgenoessischen Tech. Hochschule, Zurich, CH-8092, Switz.). Helv. Chim. Acta, 78(2), 292-300 (English) 1995. CODEN: HCACAV. ISSN: 0018-019X.
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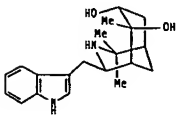

I

AB Synthetic (+)-makomakine was transformed in six steps into (+)-(17R,18R)-17,18-dihydrohobartine-17,18-diol ((+)-1) with an overall yield of 38%. This compd. was shown to be identical with natural hobartinol, a monoterpene indole alkaloid from Aristotelia australasica, originally believed to be the (17S)-epimer. At the same time, the synthesis of (+)-1 delineates the hitherto unknown abs. configuration of this metabolite.
IT 131669-90-4P, (+)-Hobartinol
RL: PRP (Properties); SPN (Synthetic preparation); PREP (Preparation)
(total synthesis of hobartinol)
IT 79559-56-1, (+)-Makomakine
RL: RCT (Reactant)
(total synthesis of hobartinol)
IT 163812-29-1P 163812-32-6P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)
(total synthesis of hobartinol)
IT 163812-33-7P 163956-17-0P
RL: SPN (Synthetic preparation); PREP (Preparation)
(total synthesis of hobartinol)

L6 ANSWER 11 OF 180 CAPLUS COPYRIGHT 1996 ACS
1995:502550 Document No. 123:228024 Trapping of iminiums by the indole nucleus during catalytic hydrogenation of nitriles: a rapid synthesis of tetrahydro-.beta.-carbolines. Diker, Khalid; Doee de Maindreville, Michele; Levy, Jean (Faculte Pharmacie, Universite Reims Champagne-Ardenne, Reims, F-51096, Fr.). Tetrahedron Lett., 36(14), 2497-500 (English) 1995. CODEN: TELEAY. ISSN: 0040-4039.
AB Reductive self-condensation of indoleacetonitrile upon catalytic hydrogenation over Pd-C in acetic acid yielded 1-(3-indolylmethyl)-1,2,3,4-tetrahydro-.beta.-carboline. Hydrogenating 3,4-dimethoxyphenylacetonitrile failed to give tetrahydropapaverine, but a cross reaction between indoleacetonitrile and 3,4-dimethoxyphenylacetonitrile allowed isolation of 1-(3,4-dimethoxybenzyl)-1,2,3,4-tetrahydro-.beta.-carboline, which was also prepd. (76 %) by catalytic hydrogenation of a mixt. of tryptamine and 3,4-dimethoxyphenylacetonitrile. Besides an easy access to the yohimbane skeleton, the reaction opens the way to a useful general synthesis of tetrahydro-.beta.-carbolines.
IT 168209-33-4P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)
(synthesis of tetrahydrocarbolines by catalytic hydrogenation of nitriles)
IT 168209-35-6P
RL: SPN (Synthetic preparation); PREP (Preparation)
(synthesis of tetrahydrocarbolines by catalytic hydrogenation of nitriles)

L6 ANSWER 12 OF 180 CAPLUS COPYRIGHT 1996 ACS
1995:466381 Document No. 122:256183 The pre- and postjunctional activity of CP-122,288, a conformationally restricted analog of sumatriptan. Beattie, David T.; Connor, Helen E. (Pharmacology II, Glaxo Research and Development Ltd., Park Road, Ware Herts, SG12 0DP, UK). Eur. J. Pharmacol., 276(3), 271-6 (English) 1995. CODEN: EJPHAZ. ISSN: 0014-2999.
AB The present study investigated the pre- and postjunctional activity of CP-122,288 (5-methyl-aminosulfonylmethyl-3-(N-methylpyrrolidin-2R-yl-methyl)-1H -indole), an analog of the vascular 5-HT1 receptor agonist, sumatriptan. CP-122,288 inhibited neurogenic plasma protein extravasation in rat dura with a potency approx. 40 000-fold greater than sumatriptan (ID50 values of 0.3 pmol/kg and 13.9 nmol/kg i.v. resp.). However, CP-122,288 was only approx. 2-fold more potent than sumatriptan at inhibiting neurogenically mediated contractions of the dog saphenous vein. CP-122,288 contracted the dog saphenous vein and basilar artery with a potency approx. 2-fold greater than that of sumatriptan. Both compds. possessed similar affinities at either human 5-HT1D.alpha. or 5-HT1D.beta. receptors. It is concluded that CP-122,288 exhibits a prejunctional selectivity in the meninges to inhibit dural plasma protein extravasation independent of 5-HT1D.alpha. and 5-HT1D.beta. receptor activation.
IT 143321-74-8, CP-122288
RL: BAC (Biological activity or effector, except adverse); BIOL (Biological study)
(pre- and postjunctional activity of CP-122,288, a conformationally restricted analog of sumatriptan)

L6 ANSWER 13 OF 180 CAPLUS COPYRIGHT 1996 ACS
1995:421524 Document No. 122:205025 Suppression by the sumatriptan analog, CP-122,288 of c-fos immunoreactivity in trigeminal nucleus caudalis induced by intracisternal capsaicin. Cutrer, F. Michael; Schoenfeld, David; Limmroth, Volker; Panahian, Mariman; Moskowitz, Michael A. (Harvard Med. Sch., Massachusetts Gen. Hosp., Boston, MA, 02114, USA). Br. J. Pharmacol., 114(5), 987-92 (English) 1995. CODEN: BJPCBM. ISSN: 0007-1188.
AB The effects of an i.v. administered sumatriptan analog were exmd. on c-fos-like immunoreactivity (c-fos-LI), a marker of neuronal activation, evoked within trigeminal nucleus caudalis (TNC) and other brain stem regions 2 h after intracisternal injection of the irritant, capsaicin (0.1 mo, 0.1 nM), in pentobarbitone-anesthetized Hartley guinea pigs. C-fos-LI was assessed in eighteen serial sections (50 .mu.m) using a polyclonal antiserum. A weighted av., reflecting total expression within lamina I, IIO of TNC was obtained from three representative levels (i.e., at -0.225 mm, -2.475 mm and -6.075 mm). Capsaicin caused significant labeling within lamina I, IIO, a region contg. axonal terminatns of small unmyelinated C-fibers, as well as within the nucleus of the solitary tract, area postrema and medial reticular nucleus. A similar distribution of pos. cells was reported previously after intracisternal injection of other chem. irritants such as autologous blood or carrageenin. Pretreatment with a conformationally restricted sumatriptan analog (with some selectivity for 5-HT1B and 5-HT1D receptor subtypes) CP-122,288, reduced the weighted av. by approx. 50-60% ($P < 0.05$) in lamina I, IIO at 100 pmol kg-1, i.v., but did not decrease cell no. within area postrema, nucleus of the solitary tract or medical reticular nucleus. A similar pattern was reported previously following sumatriptan, dihydroergotamine or CP-93,129 administration after noxious meningeal stimulation. We conclude that modifications at the amino-Et side chain of sumatriptan dramatically enhance the suppression of c-fos expression within TNC, a finding consistent with its remarkable potency against neurogenic plasma protein extravasation within dura matter. CP-122,288 and related analogs may serve as an important prototype for drug development in migraine and related headaches.
IT 143321-74-8, CP-122288
RL: BAC (Biological activity or effector, except adverse); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(suppression by sumatriptan analog, CP-122,288 of c-fos immunoreactivity in trigeminal nucleus caudalis induced by intracisternal capsaicin)

L6 ANSWER 14 OF 180 CAPLUS COPYRIGHT 1996 ACS
1995:373949 Document No. 122:240108 Microbial hydroxylation of some synthetic Aristotelia alkaloids. Dobler, Markus; Borschberg, Hans-Juerg (Lab. Org. Chem., Eidgenoesschen Tech. Hochsch., Zurich, CH-8092, Switz.). Tetrahedron: Asymmetry, 6(1), 213-20 (English) 1995. CODEN: TASYEJ. ISSN: 0957-4166. OTHER SOURCES: CASREACT 122:240108.
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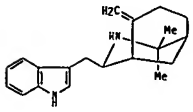
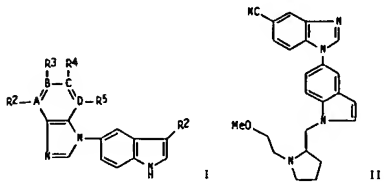


I

AB Synthetically prepd., optically pure samples of the rare Aristotelia alkaloids (+)-makomakine (I), (-)-hobartine, and (+)-aristoteline, were exposed to twelve selected fungal strains and have been shown to afford, sometimes in preparatively acceptable yield, known, as well as hitherto unknown hydroxylated derivs. thereof.
IT 162333-71-3P 162333-72-4P 162333-73-5P
162428-48-0P
RL: BPN (Biosynthetic preparation); BIOL (Biological study); PREP (Preparation)
(microbial hydroxylation of some synthetic Aristotelia alkaloids)
IT 73004-61-2, (-)-Hobartine 79559-56-1,
(+)-Makomakine
RL: RCT (Reactant)
(microbial hydroxylation of some synthetic Aristotelia alkaloids)

L6 ANSWER 15 OF 180 CAPLUS COPYRIGHT 1996 ACS (Continued)
160906-86-5P 160906-87-6P 160906-95-6P
160906-96-7P 160906-97-8P 160907-00-6P
160907-08-4P
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of, as intermediate for arylindole serotoninergic agonist)
IT 160906-56-9P 160906-57-0P 160906-58-1P
160906-59-2P 160906-60-5P 160906-61-6P
160906-62-7P 160906-63-8P 160906-64-9P
160906-65-0P 160906-66-1P 160906-68-3P
160906-69-4P 160906-72-9P 160906-73-0P
160906-74-1P 160906-75-2P 160906-79-6P
160906-80-9P 160906-91-2P 160906-94-5P
160907-03-9P
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of, as serotoninergic agonist)
IT 151272-88-7
RL: RCT (Reactant)
(reactant for arylindole serotoninergic agonist)
IT 160907-09-5
RL: RCT (Reactant)
(serotoninergic agonist)

L6 ANSWER 15 OF 180 CAPLUS COPYRIGHT 1996 ACS
1995:354225 Document No. 122:133200 5-arylindole derivatives and their use as serotonin (5-HT1) agonists. Macor, John Eugene (Pfizer Inc., USA). PCT Int. Appl. WO 9410171 A1 940511, 72 pp. DESIGNATED STATES: W: AU, BR, CA, CZ, JP, KR, NO, NZ, PL, RU, US; RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE. (English). CODEN: PIXXD2. APPLICATION: WO 93-US9790 931019. PRIORITY: US 92-970758 921102.
GI

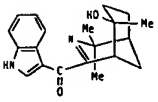


I II

AB The title compds. I (R1 = aminoalkyl; R2-R5 = H, alkyl, aryl, etc.) were disclosed. I are useful in treating migraine and other disorders; they are useful psychotherapeutics and are potent serotonin (5-HT1) agonists and benzodiazepine agonists and antagonists and may be used in the treatment of depression, anxiety, eating disorders, obesity, drug abuse, cluster headache, migraine, pain and chronic paroxysmal hemicrania and headache assocd. with vascular disorders, and other disorders arising from deficient serotonergic neurotransmission. I are also useful as centrally acting antihypertensives and vasodilators. A specifically claimed example compd. is 5-cyano-1-[[3-[1-(2-methoxyethyl)-2-pyrrolidinyl]methyl]-5-indolyl]-1H-benzimidazole (II).
IT 160907-04-0P 160907-05-1P 160907-06-2P
160907-07-3P
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of)
IT 143322-01-4P 151272-89-8P 151272-90-1P
151272-99-0P 151273-00-6P 151273-01-7P
151273-05-1P 151273-06-2P 151273-07-3P
151273-08-4P 151273-11-9P 158752-53-5P
160906-44-5P 160906-45-6P 160906-46-7P
160906-47-8P 160906-48-9P 160906-49-0P
160906-50-3P 160906-51-4P 160906-54-7P
160906-55-8P 160906-81-0P 160906-82-1P
160906-83-2P 160906-84-3P 160906-85-4P

L6 ANSWER 16 OF 180 CAPLUS COPYRIGHT 1996 ACS
1995:300051 Document No. 122:64328 Use of indole derivatives as 5-HT1 antagonists. Macor, John Eugene (Pfizer Inc., USA). PCT Int. Appl. WO 9425023 A1 941110, 22 pp. DESIGNATED STATES: W: AU, BG, BR, CA, CN, CZ, FI, HU, JP, KR, NO, NZ, PL, RO, RU, SK; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, DE, DK, ES, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG. (English). CODEN: PIXXD2. APPLICATION: WO 94-IB79 940426. PRIORITY: US 93-53930 930427.
AB The present invention relates to pharmaceutical compns. contg. (R)-5-(methylaminosulfonylmethyl)-3-(N-methylpyrrolidin-2-ylmethyl)-1H-indole or (R)-5-(methylaminosulfonylmethyl)-3-(pyrrolidin-2-ylmethyl)-1H-indole for the treatment of conditions such as hypertension, depression, anxiety, eating disorders, obesity, drug abuse, cluster headache, migraine, pain, chronic paroxysmal hemicrania, and headache assocd. with vascular disorders.
IT 143321-82-8P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)
(indole derivs. for treatment of disorders from deficient serotonergic neurotransmission)
IT 143321-74-8P 143321-78-2P
RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(indole derivs. for treatment of disorders from deficient serotonergic neurotransmission)

L6 ANSWER 17 OF 180 CAPLUS COPYRIGHT 1996 ACS
1995:191714 Document No. 122:106219 Synthesis of Aristotelia-type alkaloids. Part XIV. total synthesis of (+)-aristolone. Dobler, Markus; Borschberg, Hans-Juerg (Lab. Org. Chem., Eidgenoessischen Technischen Hochschule, Zurich, CH-8092, Switz.). Tetrahedron: Asymmetry, 5(10), 2025-32 (English) 1994. CODEN: TASYE3. ISSN: 0957-4166. OTHER SOURCES: CASREACT 122:106219.
GI



I

AB The first total synthesis of the highly functionalized monoterpenoid indole alkaloid (+)-aristolone (I) is described. This investigation uncovered the hitherto unknown relative and abs. configuration of this rare metabolite which had been isolated before by others in ppm-amts. from Aristotelia australasica. Dehydration of synthetic I led to a readily separable mixt. of the two alkaloids 11,12-didehydro-1-oxomakomakine and 11,12-didehydro-1-oxohobartine which had been isolated in 1988 from A. chilensis.
IT 79559-56-1P, (+)-Makomakine
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)
(total synthesis of aristolone)
IT 99655-77-3P 159979-19-8P 159979-26-7P
RL: SPN (Synthetic preparation); PREP (Preparation)
(total synthesis of aristolone)

L6 ANSWER 18 OF 180 CAPLUS COPYRIGHT 1996 ACS
1995:115157 Document No. 122:9327 Stoichiometrically sensitized decarboxylation occurring in a mol. crystal composed of phenanthridine and 3-indoleacetic acid. Koshiba, Hideko; Ding, Kuilling; Matsuura, Teruo (Fac. Sci. Technology, Ryukoku Univ., Otsu, 520-21, Japan). J. Chem. Soc., Chem. Commun. (18), 2053-4 (English) 1994. CODEN: JCCCAT. ISSN: 0022-4936. OTHER SOURCES: CJRSC.
AB Irradn. of a mol. crystal between phenanthridine and 3-indoleacetic acid at -70.degree.C causes decarboxylation to give 3-methylindole in high yield as the sole product; phenanthridine behaves like a stoichiometric sensitizer in the crystal.
IT 159617-53-5P
RL: BYP (Byproduct); PREP (Preparation)
(stoichiometrically sensitized decarboxylation occurring in a mol. crystal composed of phenanthridine and indoleacetic acid)

L6 ANSWER 19 OF 180 CAPLUS COPYRIGHT 1996 ACS
1994:681120 Document No. 121:281120 The synthesis of .alpha.-(3-indolylmethyl)proline-containing compounds as CCK ligands: analogs of PD-134308. Kendrick, David A.; Ryder, Hamish; Semple, Graeme; Sheppard, Andrew; Szelke, Michael (Res. Cent., Southampton Univ., Southampton, SO1 7NP, UK). Pept. 1992, Proc. Eur. Pept. Symp., 22nd, Meeting Date 1992, 579-80. Editor(s): Schneider, Conrad H.; Eberle, Alex N. ESCOM: Leiden, Neth. (English) 1993. CODEN: 60LUAM.
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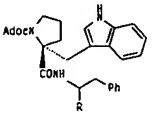

I

AB A report from a symposium on the stereoselective prepn. of analogs I (Adoc = 2-adamantyloxycarbonyl) which have and .alpha.-(3-indolylmethyl)proline residue in place of the .alpha.-methyl-D-tryptophan of PD 134308.
IT 158873-11-1DP, peptides contg.
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)
(asym. synthesis of .alpha.-(3-indolylmethyl)proline-contg. peptides as analogs of PD 134308)
IT 158873-12-2DP, derivs.
RL: SPN (Synthetic preparation); PREP (Preparation)
(asym. synthesis of .alpha.-(3-indolylmethyl)proline-contg. peptides as analogs of PD 134308)

L6 ANSWER 20 OF 180 CAPLUS COPYRIGHT 1996 ACS
1994:680497 Document No. 121:280497 Use of 2,5-Dimethylpyrrole as an Amino-Protecting Group in an Efficient Synthesis of 5-Amino-3-[(N-methyl- pyrrolidin-2(R)-yl)methyl]indole. Macor, John E.; Chenard, Bert L.; Post, Ronald J. (Department of Medicinal Chemistry, Pfizer Inc., Groton, CT, 06340, USA). J. Org. Chem., 59(24), 7496-8 (English) 1994. CODEN: JOCEAH. ISSN: 0022-3263. OTHER SOURCES: CASREACT 121:280497; CJACS-IMAGE; CJACS.
AB 5-Amino-3-(N-methylpyrrolidin-2R-ylmethyl)indole was synthesized in an overall of 39% in four steps on a large scale. Crucial to the success of this sequence was the use of a 2,5-dimethylpyrrole as the protecting group for the 5-aminoindole functionality. This protecting group was stable to (unreactive toward) ethylmagnesium bromide, a hindered acid chloride (CBZ-proline acid chloride), and lithium aluminum hydride, but easily removed in high yield using unique conditions (hydroxylamine hydrochloride/triethylamine/propanol/water/.DELTA.).
IT 158752-53-5P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)
(use of dimethylpyrrole as an amino-protecting group in an efficient synthesis of amino[(methylpyrrolidinyl)methyl]indole)
IT 143322-01-4P
RL: SPN (Synthetic preparation); PREP (Preparation)
(use of dimethylpyrrole as an amino-protecting group in an efficient synthesis of amino[(methylpyrrolidinyl)methyl]indole)

L6 ANSWER 21 OF 180 CAPLUS COPYRIGHT 1996 ACS
1994:631280 Document No. 121:231280 Non-decarboxylative 1,3-dipolar cycloadditions of imines of .alpha.-amino acids as a route to proline derivatives. Aly, Moustafa F.; Younes, Mansour I.; Metwally, Saoud A. M. (Fac. Sci., Assiut Univ., Qena, Egypt). Tetrahedron, 50(10), 3159-68 (English) 1994. CODEN: TETRAB. ISSN: 0040-4020. OTHER SOURCES: CASREACT 121:231280.
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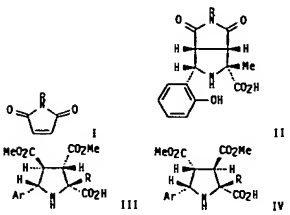
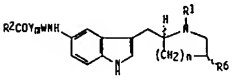


AB The 1,3-dipolar cycloaddn. reaction of alanine with salicylaldehyde and N-substituted maleimides I (R = Me, Ph) gave stereospecific cycloadducts II. The 1,3-dipolar cycloaddn. reaction of .alpha.-amino acids with aryl aldehydes in the presence of di-Me fumarate gave isomeric cycloadducts III (Ar = 2-hydroxyphenyl, R1 = Me, H, CH2CHMe2, CH2CH2SMe, CH2Ph, indol-3-ylmethyl; Ar Ph, 2-methoxyphenyl, 2,4-dimethoxyphenyl, R1 = Me) and IV (Ar and R1 = same). The relatively low yield in the case of di-Me fumarate is presumably due to the steric interaction between the dipolarophile and the substituents at both ends of the dipole.
IT 158134-75-9P 158249-37-7P
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of)

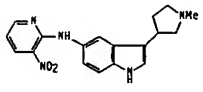
L6 ANSWER 22 OF 180 CAPLUS COPYRIGHT 1996 ACS
1994:574790 Document No. 121:174790 Antifungal substances produced by Chaetomium globosum. Asaeiya, Yoshiaiki; Kondo, Akihiro; Hirano, Kazuya; Hirukawa, Toshihusi; Kato, Tadahiro (Fac. Hortic., Chiba Univ., Matsudo, 271, Japan). Chiba Daigaku Engeigakubu Gakujutsu Hokoku, 48, 13-18 (Japanese) 1994. CODEN: CDEGAF. ISSN: 0069-3227.
AB Antifungal substances were extd. from culture filtrate of the most antagonistic isolate identified as Chaetomium globosum. Two active substances were obtained by using silica gel column chromatog. and high performance liq. chromatog. By analyzing with mass spectrometer (EIMS, HR-MS), 1H-NMR and 13C-NMR, the major substance was identified as Chaetoglobosin A, one of the toxic metabolites produced by C. globosum and C. chochliodes. Another substance was assumed to have similar structure with Chaetoglobosin A. The major substance completely inhibited the spore germination of V. dahliae at 32 .mu.g/mL. It was also active against V. albo-atrum and Rhizoctonia solani, but not against Fusarium oxysporum, F. solani and Pythium aphanidermatum.
IT 50335-03-0, Chaetoglobosin A
RL: BAC (Biological activity or effector, except adverse); BIOL (Biological study)
(from Chaetomium globosum, antifungal activity of, against Verticillium and Rhizoctonia)

L6 ANSWER 23 OF 180 CAPLUS COPYRIGHT 1996 ACS
1994:483048 Document No. 121:83048 (Acylamino)indole derivatives as 5-HT1 agonists. Macor, John E. (Pfizer Inc., USA). PCT Int. Appl. WO 9321180 A1 931028, 32 pp. DESIGNATED STATES: W: AU, BR, CA, CZ, DE, JP, KR, NO, NZ, PL, RU, SK, UA, US; RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE. (English). CODEN: PIXXD2. APPLICATION: WO 93-US1807 930304. PRIORITY: US 92-866382 920410.
GI



AB The title compds. I [R1 = H, C1-6 alkyl, C3-6 alkenyl, C3-6 alkynyl, (un)substituted aryl, etc.; R2 = CF3, C1-6 alkyl, aryl, C1-3 alkylaryl, etc.; R6 = H, OH, alkoxy, aryloxy, acylamino, etc.; W, Y = amino acid residue; m = 0, 1; n = 0-2], which are 5-HT1 agonists (no data), useful in the treatment of hypertension (no data), depression (no data), anxiety (no data), pain (no data), etc., are prepd. Thus, N-benzyloxycabonylglycine was coupled with 5-amino-3-(N-methylpyrrolidin-2R-ylmethyl)-1H-indole, producing 5-(N-benzyloxycarbonylglycyl)amino-3-(N-methylpyrrolidin-2R-ylmethyl)-1H-indole in 74% yield.
IT 143321-58-8 143322-01-4 151272-89-8
154038-83-2 154038-84-3 154038-85-4
154038-86-5
RL: RCT (Reactant)
(prepn. as serotoninergic receptor agonist)
IT 143321-58-8 143322-01-4 151273-38-0
RL: RCT (Reactant)
(reactant, in prepn. of (acylamino)indole serotoninergic receptor agonists)

L6 ANSWER 24 OF 180 CAPLUS COPYRIGHT 1996 ACS
1994:473079 Document No. 121:73079 5-[(3-Nitropyrid-2-yl)amino]indoles: Novel Serotonin Agonists with Selectivity for the 5-HT1D Receptor. Variation of the C3 Substituent on the Indole Template Leads to Increased 5-HT1D Receptor Selectivity. Macor, John E.; Blank, David H.; Fox, Carol B.; Lebel, Lorraine A.; Newman, Michael E.; Post, Ronald J.; Ryan, Kevin; Schmidt, Anne W.; Schulz, David W.; Koe, B. Kenneth (Department of Medicinal Chemistry, Pfizer Inc., Groton, CT, 06340, USA). J. Med. Chem., 37(16), 2509-12 (English) 1994. CODEN: JMCMAR. ISSN: 0022-2623. OTHER SOURCES: CASREACT 121:73079; CJACS-IMAGE; CJACS.
GI



AB A series of 5-(3-nitropyrid-2-ylamino)indoles () has been synthesized which contain 2-aminoethyl side chains at C3 of the indole with varying degrees of conformational constraint. These compds. show different degrees of selectivity for the 5-HT1D receptor, depending on the C3 substituent. The major effect on binding and functional activity appears to be with variation of affinity and potency for the 5-HT1D receptor. The compd. most selective for the 5-HT1D receptor in this series is I.
IT 143321-58-8P 151273-38-0P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)
(prepn. and deprotection of)
IT 143322-01-4P 151272-89-8P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)
(prepn. and reaction of, with chloronitropyridine)
IT 151272-88-7P 151272-90-1P
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. and serotoninergic 5ID-agonist activity of, structure in relation to)

L6 ANSWER 25 OF 180 CAPLUS COPYRIGHT 1996 ACS
1994:457330 Document No. 121:57330 Preparation of indole derivatives as 5-HT1-like agonists. Macor, John Eugene; Wythes, Martin James (Pfizer Ltd., UK; Pfizer Inc.; Pfizer Research and Development Co., N.V./S.A.). PCT Int. Appl. WO 9321177 A1 931028, 70 pp. DESIGNATED STATES: W: AU, BR, CA, CZ, FI, HU, JP, KR, NO, NZ, PL, RU, SK, UA, US; RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE. (English). CODEN: PIXXD2. APPLICATION: WO 93-EP738 930325. PRIORITY: GB 92-7930 920410.

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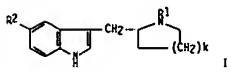

I

AB Title compds. I [R1 = (C1-6 acyl)-C1-3 alkylene, (C1-6 alkyl-O2C)-C1-3 alkylene, (H2NOC)-C1-3 alkylene, (H2NO2S)-C1-3 alkylene, (HO) C3-7 cycloalkyl, (aryl) C3-6 alkenyl, heteroaryl-C1-3 alkylene etc.; R2 = H, halo, F3C, NC, H2NOC, HO, etc.; k = 0-2] or a salt thereof, are prepd. 5-(2-Ethylsulfonylethyl)-3-(2R-pyrrodinylmethyl)-1H-indole (prepn. given) was reacted with 2-pyridylmethyl chloride to give I (R1 = 2-pyridylmethyl, R2 = 2-EtSO2CH2CH2, k = 1). A similar prepd. I (R1 = EtCOCH2, R2 = EtSO2CH2CH2, k = 1) evaluated for max. contraction on saphenous vein strip showed an EC50 = 3.1 .times. 10-3M.

IT 143322-48-9P 153435-71-3P 153525-51-0P
153525-52-1P 153525-53-2P 153525-54-3P
153525-55-4P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)
(prepn. and reaction of, prepn. of 5-HT1 agonists)

IT 143322-46-7P 143322-47-8P 153525-57-6P
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of)

IT 153435-72-4P 153435-73-5P 153525-10-1P
153525-11-2P 153525-12-3P 153525-13-4P
153525-14-5P 153525-15-6P 153525-16-7P
153525-17-8P 153525-18-9P 153525-19-0P
153525-20-3P 153525-21-4P 153525-22-5P
153525-23-6P 153525-24-7P 153525-25-8P
153525-26-9P 153525-27-0P 153525-28-1P
153525-29-2P 153525-30-5P 153525-31-6P
153525-32-7P 153525-33-8P 153525-34-9P
153525-35-0P 153525-36-1P 153525-37-2P
153525-38-3P 153525-39-4P 153525-40-7P
153525-41-8P 153525-42-9P 153525-43-0P
153525-44-1P 153525-45-2P 153525-46-3P
153525-47-4P 153525-48-5P 153525-49-6P

L6 ANSWER 25 OF 180 CAPLUS COPYRIGHT 1996 ACS (Continued)
153525-50-9P
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of, as 5HT1 agonist)

L6 ANSWER 26 OF 180 CAPLUS COPYRIGHT 1996 ACS
1994:298634 Document No. 120:298634 Preparation of imidazole, triazole, and tetrazole derivatives as 5-HT1-like receptor agonists. Castro Pineiro, Jose Luis; Castro, Pineiro Jose Luis; Guiblin, Alexander Richard; Matassa, Victor Giulio; Reeve, Austin John; Sternfeld, Francine; Street, Leslie Joseph (Merck Sharp and Dohme Ltd., UK). PCT Int. Appl. WO 9402477 A1 940203, 83 pp. DESIGNATED STATES: W: AU, CA, JP, US; RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE. (English). CODEN: PIXXD2. APPLICATION: WO 93-GB1495 930715. PRIORITY: GB 92-15721 920724; GB 92-25657 921208.

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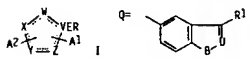

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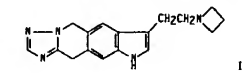

I

AB Title compds. [I; the broken circle represents two non-adjacent double bonds in any position in the five-membered ring; A1 = H, hydrocarbyl, heterocyclyl, halo, etc.; A2 = groups cited for A1, etc.; E = bond, alkylene; R = heteroaryl group Q; B = O, S, NR3; R1 = 2-pyrrolidinoethyl, 3-aminocyclobutyl, 3-pyrrolidinylmethyl, etc.; U = N, CR2; R2,R3 = H, alkyl; 2-4 of V,W,X,Y,Z = N and the other(s) = C (sic)] were prepd. Thus, 1-(4-hydrazinophenyl)methyl-1,2,4-triazole and 4-(1-azetidinyl)butanal di-Me acetal (prepn. each given) were subjected to Fischer indole synthesis conditions to give title compd. II. I had pEC50 of .gtoreq.5.0 for mediation of rabbit saphenous vein contraction.

IT 154748-38-6P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)
(prepn. and reaction of, in prepn. of 5-HT1-like receptor agonist)

IT 154748-36-4P 154748-37-5P 154748-39-7P
154804-04-3P
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of, as 5-HT1-like receptor agonist)

L6 ANSWER 27 OF 180 CAPLUS COPYRIGHT 1996 ACS
1994:217347 Document No. 120:217347 The synthesis of conformationally/rotationally restricted analogs of the neurotransmitter serotonin. Macor, John E.; Blank, David H.; Post, Ronald J. (Cent. Res. Div., Pfizer Inc., Groton, CT, 06340, USA). Tetrahedron Lett., 35(1), 45-8 (English) 1994. CODEN: TELEAY. ISSN: 0040-4039. OTHER SOURCES: CASREACT 120:217347.

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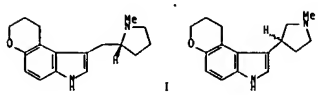
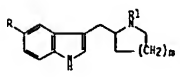


I II

AB The novel conformationally/rotationally restricted analogs I and II of the neurotransmitter serotonin which are modeled after the 5-HT2 receptor selective agonist CP-143,474 [a dihydropyrano[3,2-e]indole] were prepd.are described. I was obtained from the pyranoindole and II from 5-indolol.

IT 153969-85-8P
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of)

L6 ANSWER 28 OF 180 CAPLUS COPYRIGHT 1996 ACS
1994:217271 Document No. 120:217271 Indole derivatives as 5-HT1 agonists. Brown, Alan Daniel; Dickinson, Roger Peter; Wythes, Martin James (Pfizer Ltd., UK; Pfizer Inc.; Pfizer Research and Development Co., N.V./S.A.). PCT Int. Appl. WO 9321178 A1 931028, 146 pp. DESIGNATED STATES: W: AU, BR, CA, CZ, FI, HU, JP, KR, NO, NZ, PL, RU, SK, UA, US; RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE. (English). CODEN: PIXXD2. APPLICATION: WO 93-EP867 930408. PRIORITY: GB 92-8161 920414.
GI

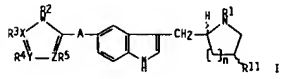


I

AB The title compds. I [R = (un)substituted Ph, pyridinyl, pyridazinyl, pyrimidinyl, pyrazinyl, furyl, thienyl; R1 = H, C1-6 alkyl, C3-7 cycloalkyl, C5-7 cycloalkenyl, C3-6 alkenyl, C3-6 alkynyl, etc.; m = 1, 2], which are selective agonists at the 5-HT1-like subtype of the 5-hydroxytryptamine receptor, are prepd. Thus, I (R = 3-C6H4SO2NH2, R1 = Me, m = 1) was prepd. and demonstrated 50% max. contraction of dog-isolated saphenous vein strip at 3.78 X 10-9 M.
IT 153434-62-9 153434-63-0 153434-64-1
153434-65-2 153434-66-3 153434-67-4
153434-68-5 153434-69-6 153434-70-9
153434-71-0 153434-72-1 153434-73-2
153434-74-3 153434-75-4 153434-76-5
153434-77-6 153434-78-7 153434-79-8
153434-80-1 153434-81-2 153434-82-3
153434-83-4 153434-84-5 153434-85-6
153434-86-7 153434-87-8 153434-88-9
153434-89-0 153434-90-3 153434-91-4
153434-92-5 153434-93-6 153434-94-7
153434-95-8 153434-96-9 153434-97-0
153434-98-1 153434-99-2 153435-00-8
153435-01-9 153435-02-0 153435-03-1
153435-04-2 153435-05-3 153435-06-4
153435-07-5 153435-08-6 153435-09-7
153435-10-0 153435-11-1 153435-12-2
153435-13-3 153435-14-4 153435-15-5
153435-16-6 153435-17-7 153435-18-8
153435-19-9 153435-20-2 153435-21-3
153435-22-4 153435-23-5 153435-24-6
153435-25-7 153435-26-8
RL: RCT (Reactant)
(prepn. as 5-HT1 receptor agonist)
IT 143322-46-7 143322-57-0 153435-54-2
153435-55-3 153435-56-4 153435-57-5
153435-58-6 153435-71-3 153435-72-4

L6 ANSWER 28 OF 180 CAPLUS COPYRIGHT 1996 ACS (Continued)
153435-73-5
RL: RCT (Reactant)
(prepn. as intermediate in prepn. of 5-HT1 receptor agonists)

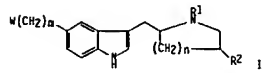
L6 ANSWER 29 OF 180 CAPLUS COPYRIGHT 1996 ACS
1994:106995 Document No. 120:106995 Preparation of azole indole derivatives as 5-HT1 agonists. Macor, John E.; Nowakowski, Jolanta T. (Pfizer Inc., USA). PCT Int. Appl. WO 9318032 A1 930916, 38 pp. DESIGNATED STATES: W: AU, BR, CA, CZ, DE, JP, KR, NO, NZ, PL, RU, SK, UA, US; RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE. (English). CODEN: PIXXD2. APPLICATION: WO 93-US1667 930303. PRIORITY: US 92-846640 920305.
GI



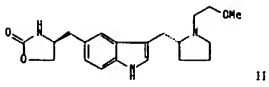
I

AB Title compds. I (A = bond, C1-4 alkyl, C1-4 alkenyl; n = 0-2; R1 = H, C1-6 alklaryl, aryl, C1-3 alkylheteroaryl, R6(CH2)m wherein R6 = NC, F3C, etc., m = 1-3; W, X, Y, Z = O, S, N, C such that at least one of W, X, Y, Z is N; R2, R3, R4, R5 = H, O1-6 alkyl, aryl, C1-3 alkylaryl, C1-3 alkylheteroaryl, halo, NC, F3C, O2N, etc.; one of R2R3, R3R4, R4R5 = 5-7-membered alkyl ring, 6-membered alkyl ring, 5-7-membered heteroalkyl having 1 of O, N, S, etc.; R11 = H, R12O, R12OHN wherein R12 = C1-6 alkyl, aryl, C1-3 alkylaryl) an a salt thereof useful as 5-HT, agonists (no data) and in disorders arising from deficient serotoninergic neurotransmission (no data), are prepd. (R)-I (A = bond, n = 1, R1 = PhCH2O2C, W = S, Z = N, X = Y = C, R2 = R3 = R11 = H, R4 = PhCH2) (prepn. given) in THF was treated with LiAlH4 to give (R)-I (A = bond, n = 1, R1 = Me, W = S, Z = N, X = Y = C, R2 = R3 = R11 = H, R4 = PhCH2).
IT 152362-19-1P 152362-20-4P 152362-21-5P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)
(prepn. and reaction of, in prepn. of 5-HT1 agonist)
IT 152362-15-7P 152362-16-8P 152362-17-9P
152362-18-0P 152362-32-8P 152362-33-9P
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of, as 5-HT1 agonist)

L6 ANSWER 30 OF 180 CAPLUS COPYRIGHT 1996 ACS
1994:106761 Document No. 120:106761 Indole derivatives as serotonin receptor (5-HT1) agonists. Macor, John E.; Wythes, Martin J. (Pfizer Inc., USA). PCT Int. Appl. WO 9320073 A1 931014, 43 pp. DESIGNATED STATES: W: AU, BR, CA, CZ, DE, JP, KR, NO, NZ, PL, RU, SK, UA, US; RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE. (English). CODEN: PIXXD2. APPLICATION: WO 93-US1967 930310. PRIORITY: US 92-864737 920407.
GI



I

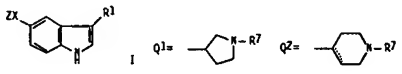


II

AB Three members of claimed indoles I [n = 0-2; m = 0-3; W = 7 types of oxo- and/or thioxo-substituted azolidinyl radicals (pyrrolidinyl, imidazolidinyl, oxazolidinyl, thiazolidinyl) with optional addnl. substitutents; R1 = H, (hydroxy)alkyl, alkenyl, alkynyl, aryl, alkylaryl (sic, e.g., CH2Ph), alkylheteroaryl, certain heterofunctional-terminated alkyl; R2 = H, OR3, NHCOR3; R3 = H, , alkyl, aryl, alkylaryl], potent 5-HT1 agonists (no data), were prepd. for treatment of hypertension, depression, anxiety, obesity, migraine, etc. For example, Mitsunobu coupling of the alc. (R)-1-(N-benzyloxycarbonylpyrrolidin-2-yl)-3-hydroxypropene with 2-brono-4-(2-oxo-1,3-oxazolidin-4(S)-ylmethyl)-1-(trifluoroacetylamino)benzene at the amide N (100% yield), followed by Pd(OAc)2-catalyzed cyclization to an indole (40%), hydrogenolytic deprotection (89%), and N-alkylation with MeOCH2CH2Br (36%), gave title compd. II.
IT 143322-57-0P
RL: SPN (Synthetic preparation); PREP (Preparation)
(Pd-catalyzed coupling; prepn. of indole derivs. as 5-HT1 agonists)
IT 152305-14-1P 152305-19-6P 152305-20-9P
152305-21-0P 152305-24-3P 152305-25-4P
RL: SPN (Synthetic preparation); PREP (Preparation)
(intermediate; prepn. of indole derivs. as 5-HT1 agonists)
IT 152305-12-9P 152305-13-0P 152305-22-1P
152305-26-5P
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of indole derivs. as 5-HT1 agonists)

L6 ANSWER 31 OF 180 CAPLUS COPYRIGHT 1996 ACS
1993:662341 Document No. 119:262341 Conformationally restricted sumatriptan analogs, CP-122,288 and CP-122,638 exhibit enhanced potency against neurogenic inflammation in dura mater. Lee, Won Suk; Moskowitz, Michael A. (Stroke Research Laboratory, Neurosurgery and Neurology Services, Massachusetts General Hospital, Harvard Medical School, 32 Fruit Street, Boston, MA, 02114, USA). Brain Res., 626(1-2), 303-5 (English) 1993. CODEN: BRREAP. ISSN: 0006-8993.
AB CP-122,288 and CP-122,638 (analogs of sumatriptan in which the C3-aminoethyl side chain has been modified) blocked plasma protein extravasation response within dura mater following trigeminal ganglion stimulation. The threshold (1 and 0.1 pmol/kg, resp.) was remarkably lower than for sumatriptan (7 nmol/kg), as was the dose at max. response. As with sumatriptan, substance P-induced plasma leakage was unaffected by either compd., and metergoline only partially (27%) reversed the effects of CP-122,288. The data suggest the importance of modifications at the aminoethyl side chain to the actions of sumatriptan and possibly to the treatment of migraine headache.
IT 143321-74-8, CP 122288 143321-78-2, CP 122638
RL: BIOL (Biological study)
(neurogenic pachymeningitis-inhibition by, structure in relation to)

L6 ANSWER 32 OF 180 CAPLUS COPYRIGHT 1996 ACS
1993:649833 Document No. 119:249833 Indole derivatives which are potent serotinin receptor antagonists. Macor, John E. (Pfizer Inc., USA). PCT Int. Appl. WO 9311106 A1 930610, 65 pp. DESIGNATED STATES: W: AU, BR, CA, CS, DE, FI, HU, JP, KR, NO, PL, RU, UA, US; RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, SE. (English). CODEN: PIXXD2. APPLICATION: WO 92-US8306 921006. PRIORITY: US 91-796744 911125.
GI

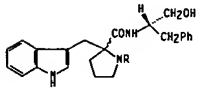


I

AB The title compds. I [R1 = CH2CH2NR7R8, Q1, Q2 (dotted line represents an optional double bond), etc.; R7,R8 = H, C1-6alkyl, aryl, C1-3alkylaryl, etc.; X = O, NH, S; Z = (un)substituted 5- or 6-membered heterocycleo; R7R8 may form a 4- to 6-membered ring], which are potent serotonin (5-HT1) receptor antagonists (no data), useful in the treatment of hypertension (no data), depression (no data), anxiety (no data), eating disorders (no data), obesity (no data), etc., are prepd. Thus, (R)-5-amino-3-(pyrrolidin-2-ylmethyl)-1-H-indole was prepd. by hydrogenolysis of (R)-3-(N-benzyloxycarbonylpyrrolidin-2-ylmethyl)-5-dibenzylamino-1H-indole.
IT 143321-58-8P 143322-01-4P 151272-88-7P
151272-89-8P 151272-90-1P 151272-99-0P
151273-00-6P 151273-01-7P 151273-02-8P
151273-03-9P 151273-04-0P 151273-05-1P
151273-06-2P 151273-07-3P 151273-08-4P
151273-09-5P 151273-11-9P 151273-12-0P
151273-13-1P 151273-14-2P 151273-15-3P
151273-16-4P 151273-17-5P 151273-18-6P
151273-19-7P 151273-20-0P 151273-21-1P
151273-38-0P 151273-42-6P 151273-44-8P
151273-46-0P 151273-48-2P 151305-77-0P
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. and serotonin receptor antagonist activity of)
IT 143322-68-3 151273-10-8
RL: RCT (Reactant)
(reaction of, in prepn. of indole serotonin receptor antagonist)

L6 ANSWER 33 OF 180 CAPLUS COPYRIGHT 1996 ACS
1993:510909 Document No. 119:110909 20-Ketoreductase activity of chaetoglobosin A and prochaetoglobosins in a cell-free system of Chaetomium subaffine and the isolation of new chaetoglobosins. Oikawa, Hideaki; Murakami, Yasunobu; Ichihara, Akitami (Fac. Agric., Hokkaido Univ., Sapporo, 060, Japan). Biosci., Biotechnol., Biochem., 57(4), 628-31 (English) 1993. CODEN: BBBIEJ.
AB The conversion of prochaetoglobosins as plausible precursors into mycotoxin chaetoglobosin A in a cell-free system of C. subaffine was unsuccessful. Reductase activity of the 20-keto-analogs, and prochaetoglobosins II and III were found in a microsomal fraction of this fungi. Two new metabolites of chaetoglobosins, named chaetoglobosin Fex and 20-dihydrochaetoglobosin A, were also isolated from the same microorganisms. Their structures were elucidated by spectroscopic data and chem. transformation.
IT 149457-95-4 149560-98-5
RL: PROC (Process)
(as chaetoglobosin metabolite of Chaetomium subaffine, formation of)
IT 149439-83-8 149439-84-9
RL: BIOL (Biological study)
(chaetoglobosins of Chaetomium subaffine in relation to)
IT 50335-03-0, Chaetoglobosin A
RL: BIOL (Biological study)
(ketoreductase of, of Chaetomium subaffine)
IT 133613-78-2 133625-26-0
RL: BIOL (Biological study)
(of Chaetomium subaffine, ketoreductase in relation to)

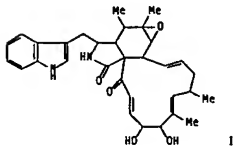
L6 ANSWER 34 OF 180 CAPLUS COPYRIGHT 1996 ACS
1993:496155 Document No. 119:96155 The use of a proline ring as a conformational restraint in CCK-B receptor dipeptoids. Fincham, Christopher I.; Horwell, David C.; Ratcliffe, Giles S.; Rees, David C. (Parke-Davis Neurosci. Res. Cent., Cambridge, CB2 2QB, UK). Bioorg. Med. Chem. Lett., 2(5), 403-6 (English) 1992. CODEN: BMCLE8. ISSN: 0960-894X.
GI



I

AB Examn. of mol. dynamics simulations and an x-ray crystal structure of a selective cholecystokinin B (CCK-B) receptor dipeptoid Trp deriv. led to the synthesis of conformationally restrained Pro deriv. I. The CCK receptor binding of I is described.
IT 149170-00-3P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)
(prepn. and amidation of, with amino(phenyl)propanol)
IT 149170-01-4P 149170-02-5P
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. and cholecystokinin B receptor binding affinity and selectivity of)

L6 ANSWER 35 OF 180 CAPLUS COPYRIGHT 1996 ACS
1993:253396 Document No. 118:253396 Immunomodulator and antitumor TAN-1142 and its manufacture with Chaetomium. Tanida, Seiichi; Tsuboya, Shigetoshi; Harada, Setsuo (Takeda Chemical Industries, Ltd., Japan). Jpn. Kokai Tokkyo Koho JP 04360691 A2 921214 Heisei, 6 pp. (Japanese). CODEN: JKXXAF. APPLICATION: JP 91-136729 910607.
GI

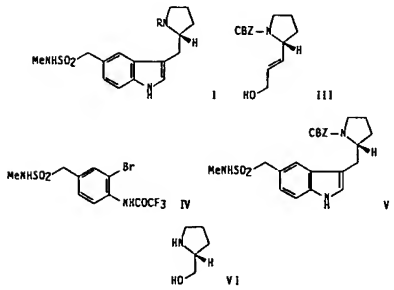


I

AB Immunomodulator and antitumor TAN-1142 (I) is manufd. by culturing I-producing Chaetomium sp. C. globosum 1-319 (IFO 32395, FERM BP-3429) was shake-cultured in a medium contg. glucose, dextrin, soybean powder, peptone, yeast ext., and salts at 28.degree. and pH 7.0 for 120 h, and the culture medium (70 L) extd. with AcOEt at pH 3.0 and processed to recover 130 mg I. I inhibited the growth of murine tumor cell B16 with 50% inhibitory concn. of 0.95 .mu.g/mL. I (at 100 mg/kg) did not show acute toxicity in mice.
IT 147527-33-1P, TAN 1142
RL: BMF (Bioindustrial manufacture); BIOL (Biological study); PREP (Preparation)
(manuf. of, with Chaetomium globosum, as immunomodulator and antitumor agent)

L6 ANSWER 36 OF 180 CAPLUS COPYRIGHT 1996 ACS
1993:251171 Document No. 118:251171 Use of HPLC diode array detection in the detection of nitrogen-containing mycotoxins and taxonomy of their producers in Penicillium. Frisvad, J. C. (Dep. Biotechnol., Technical Univ. Denmark, Lyngby, Den.). Prikl. Biokhim. Mikrobiol., 29(1), 19-26 (Russian) 1993. CODEN: PBMIAK. ISSN: 0555-1099.
AB TLC and HPLC were applied to analyze 4500 isolates from the subgenus Penicillium representing 45 species. Various systems for HPLC anal. of alkaloids are estd. The results of this estn. are presented together with a short report on taxonomy of the most widespread producers of alkaloids in Penicillium subgenus Penicillium.
IT 50335-03-0, Chaetoglobosin A
RL: FORM (Formation, nonpreparative)
(formation of, by Penicillium, taxonomy in relation to)

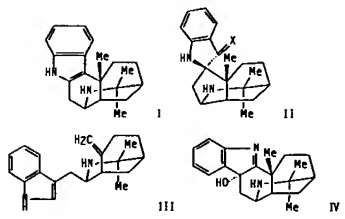
L6 ANSWER 37 OF 180 CAPLUS COPYRIGHT 1996 ACS
1993:168927 Document No. 118:168927 Synthesis of a conformationally restricted analog of the anti-migraine drug sumatriptan. Macor, John E.; Blank, David H.; Post, Ronald J.; Ryan, Kevin (Cent. Res. Div., Pfizer Inc., Groton, CT, 06340, USA). Tetrahedron Lett., 33(52), 8011-14 (English) 1992. CODEN: TELEAY. ISSN: 0040-4039. OTHER SOURCES: CASREACT 118:168927.
GI



I III IV V VI

AB The synthesis of conformationally restricted sumatriptan analog I (R = Me) (II) is described. The Mitsunobu coupling of hydroxypropene III (CBZ = benzyloxycarbonyl) with trifluoroacetanilide IV in the presence of Ph3P and DEAD gave 67% intermediate V, which underwent an intramol. Heck reaction with Pd(OAc)2 in the presence of Et3N in DMF to give 81% protected analog I (R = CBZ). A bonus of the latter cyclization was the concomitant loss of the trifluoroacetyl group. I (R = CBZ) was reduced with LiAlH4 in refluxing THF gave 65% II. III was prepd. from pyrrolidine VI in 4 steps, whereas IV was prepd. from 4-O2NC6H4CH2Cl in 6 steps.
IT 143321-74-8P
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. and antimigraine activity of)
IT 143321-82-8P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)
(prepn. and hydride redn. of)

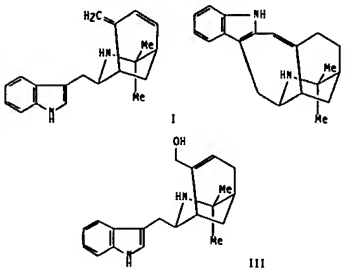
L6 ANSWER 38 OF 180 CAPLUS COPYRIGHT 1996 ACS
1993:124851 Document No. 118:124851 Total synthesis of (-)-alloaristoteline, (-)-serratoline, and (+)-aristotelone. Stoermer, Doris; Heathcock, Clayton H. (Dep. Chem., Univ. California, Berkeley, CA, 94720, USA). J. Org. Chem., 58(3), 564-8 (English) 1993. CODEN: JOCEAH. ISSN: 0022-3263. OTHER SOURCES: CASREACT 118:124851; CJACS-IMAGE; CJACS.
GI



I II III IV

AB The Aristotelia alkaloids (-)-alloaristoteline (I), (-)-serratoline, and (+)-aristotelone (II, X = O), were prepd. Thus, via the method of Stevens, (1S)-(-)-.beta.-pinene and 3-indolylacetonitrile were coupled by a Hg(NO3)2-mediated Ritter reaction followed by redn. of the resulting imine to give (+)-makomakine (III). An intramol. Friedel-Crafts reaction delivered (+)-aristoteline, which was oxidized by reaction with oxygen and platinum. Redn. of the intermediate hydroperoxide delivered alkaloid IV. Base-catalyzed skeletal rearrangement of IV followed by redn. with LiAlH4 to obtain a mixt. of secondary alcs., II (X = H,OH). Treatment of each of these alcs. with HCl in methanol afforded (-)-I.
IT 79559-56-1P, (+)-Makomakine 146144-41-4P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)
(prepn. and intramol. Friedel-Crafts reaction of)

L6 ANSWER 39 OF 180 CAPLUS COPYRIGHT 1996 ACS
1993:124830 Document No. 118:124830 Synthesis of Aristotelia-type alkaloids. Part XI. Total syntheses of (+)-sorelline and (+)-aristolasene. Dobler, Markus; Beerli, Rene; Weissmahr, Walter K.; Borschberg, Hans Juerg (Lab. Org. Chem. Eidgenoessischen Tech. Hochsch., ETH Zentrum, Zurich, CH-8092, Switz.). Tetrahedron: Asymmetry, 3(11), 1411-20 (English) 1992. CODEN: TASYE3. ISSN: 0957-4166. OTHER SOURCES: CASREACT 118:124830.
GI



AB Optically pure samples of the rare Aristotelia alkaloids (+)-sorelline (I) and (+)-aristolasene (II) were synthesized for the first time. Since natural (S)-perilla alc. served as one of the starting building blocks, these syntheses delineate the previously unknown abs. configurations of these metabolites. (-)-20-Hydroxyhobartine (III) was also prepd., which turned out to be different from a natural product that had been assigned this structure six years ago.

IT 145801-31-6P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)
(prepn. and cyclocondensation of, with tri-Et orthoformate)

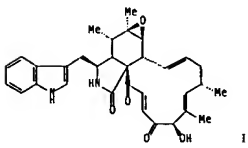
IT 146234-97-1P, (-)-20-Hydroxyhobartine
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)
(prepn. and oxidn. of)

IT 73004-61-2P, (-)-Hobartine 145801-27-0P 145842-73-5P
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of)

IT 73004-62-3P
RL: PREP (Preparation); RCT (Reactant)

L6 ANSWER 39 OF 180 CAPLUS COPYRIGHT 1996 ACS (Continued)
(synthesis of)

L6 ANSWER 40 OF 180 CAPLUS COPYRIGHT 1996 ACS
1993:120637 Document No. 118:120637 Biosynthetic study of chaetoglobosin A: origins of the oxygen and hydrogen atoms, and indirect evidence for a biological Diels-Alder reaction. Oikawa, Hideaki; Murakami, Yasunobu; Ichihara, Akitami (Fac. Agric., Hokkaido Univ., Sapporo, 060, Japan). J. Chem. Soc., Perkin Trans. 1 (21), 2955-9 (English) 1992. CODEN: JCPRB4. ISSN: 0300-922X. OTHER SOURCES: CJRSC.
GI



AB The biosynthetic origins of the O and H atoms in the mycotoxin chaetoglobosin A (I) were investigated by the incorporation of [1-13C,18O2]- and [1-13C2H3]-acetate and 18O2 into I by using the chaetoglobosin-producing strain Chaetomium subaffine. Cytochrome P 450 expts. support a biogenetic pathway from prochaetoglobosin I (II). Attempts at direct conversion of 14C- or 13C-labeled II using whole cells were unsuccessful. Formation of the diastereoisomer of II in the retro-Diels-Alder reaction of II provided indirect evidence that the plausible precursor hexaene is able to cyclize via [4 + 2]cycloaddn. in the biosynthesis of I.

IT 133613-77-1, Prochaetoglobosin I
RL: BIOL (Biological study)
(chaetoglobosin A formation from, by Chaetomium subaffine.)

IT 50335-03-0, Chaetoglobosin A
RL: FORM (Formation, nonpreparative)
(formation of, by Chaetomium subaffine, pathway of)

IT 145511-72-4P
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of)

L6 ANSWER 41 OF 180 CAPLUS COPYRIGHT 1996 ACS
1993:120537 Document No. 118:120537 Useful approach to find the plausible biosynthetic precursors of secondary metabolites using P-450 inhibitors: postulated intermediates of chaetoglobosin A. Oikawa, Hideaki; Murakami, Yasunobu; Ichihara, Akitami (Fac. Agric., Hokkaido Univ., Sapporo, 060, Japan). J. Chem. Soc., Perkin Trans. 1 (21), 2949-53 (English) 1992. CODEN: JCPRB4. ISSN: 0300-922X. OTHER SOURCES: CJRSC.
GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB Treatment of Chaetomium subaffine with specific cytochrome P 450 inhibitors resulted in a new generation of plausible precursors of chaetoglobosin A (I), named prochaetoglobosins I (II), II (III), III (IV), and IV (V), whose structures were detd. by spectroscopic anal. HPLC anal. of mycelial ext. treated with the inhibitors suggest that the accumulated metabolites are precursors in the biosynthesis of I. New less oxidized analogs, prochaetoglobosin IIIed and isochaetoglobosin J, were also isolated, and their structures were elucidated in a similar way.

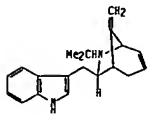
IT 146426-37-1 146426-38-2
RL: FORM (Formation, nonpreparative)
(formation of, by Chaetomium subaffine)

IT 50335-03-0, Chaetoglobosin A
RL: FORM (Formation, nonpreparative)
(formation of, by Chaetomium subaffine, cytochrome P 450 inhibitor effect on)

IT 50645-76-6 55945-75-0, Chaetoglobosin F
RL: FORM (Formation, nonpreparative)
(formation of, by Chaetomium subaffine, metyrapone effect on)

IT 133613-77-1 133613-78-2 133625-26-0 137604-97-8
RL: BIOL (Biological study)
(of Chaetomium subaffine, as potential chaetoglobosin A precursor)

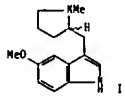
L6 ANSWER 42 OF 180 CAPLUS COPYRIGHT 1996 ACS
1993:59942 Document No. 118:59942 The alkaloid peduncularine: corrected spectroscopic data and conformational analysis. Dragar, Charles; Bick, I. Ralph C. (Dep. Agric. Sci., Univ. Tasmania, Hobart, 7005, Australia). Phytochemistry, 31(10), 3601-3 (English) 1992. CODEN: PYTCAS. ISSN: 0031-9422.
GI



I

AB The reported spectroscopic data for the alkaloid peduncularine (I) from Aristotelia peduncularis have been revised and its preferred conformation has been investigated using NOE difference spectroscopy.
IT 34964-75-5, Peduncularine 145164-88-1, Peduncularine monohydrochloride
RL: RCT (Reactant)
(cor. spectroscopic data and conformational anal.)

L6 ANSWER 43 OF 180 CAPLUS COPYRIGHT 1996 ACS
1992:651128 Document No. 117:251128 Synthesis and serotonergic pharmacology of the enantiomers of 3-[(N-methylpyrrolidin-2-yl)methyl]-5-methoxy-1H-indole: discovery of stereogenic differentiation in the aminoethyl side chain of the neurotransmitter serotonin. Macor, John E.; Blake, James; Fox, Carol B.; Johnson, Celeste; Koe, B. Kenneth; Lebel, Lorraine A.; Morrone, Jean M.; Ryan, Kevin; Schaidt, Anne W.; et al. (Cent. Res. Div., Pfizer, Inc., Groton, CT, 06340, USA). J. Med. Chem., 35(23), 4503-5 (English) 1992. CODEN: JMCMAR. ISSN: 0022-2623. OTHER SOURCES: CJACS-IMAGE; CJACS.
GI

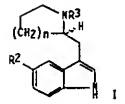


I

AB The synthesis and pharmacol. of both (R)- and (S)-3-(N-methylpyrrolidin-2-ylmethyl)-5-methoxyindole (I) are presented. Affinity for serotonergic receptors (5-HT1A, 5-HT1B, 5-HT1C, 5-HT1D, and 5-HT2) is significantly greater for (R)-I (CP-108,509). The potency and efficacy of (R)-I approx. equals that of the natural substrate serotonin at 5-HT1A, 5-HT1D, 5-HT1C, and 5-HT2 receptors. The 3-(pyrrolidin-2-ylmethyl) group in (R)-I represents a stereogenic, conformationally restricted mimic of the 3-(2-aminoethyl) group in serotonin at 5-HT1A, 5-HT1C, 5-HT1D, and 5-HT2 receptors.
IT 143321-56-6P 143321-57-7P, CP-108,509
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. and serotoninergic receptor binding by)

L6 ANSWER 44 OF 180 CAPLUS COPYRIGHT 1996 ACS
1992:610477 Document No. 117:210477 Cytochalasans and PMA induce IL-2 receptors on CD8+ lymphocytes. Grove, Deborah S.; Stanek, Elaine M.; Bour, Barbara A.; Mastro, Andrea M. (Dep. Mol. Cell Biol., Pennsylvania State Univ., University Park, PA, 16802, USA). Exp. Cell Res., 202(2), 303-9 (English) 1992. CODEN: ECREAL. ISSN: 0014-4827.
AB The cytochalasans, fungal metabolites that interact with actin, can affect lymphocyte proliferation; high concns. inhibit lectin-induced proliferation and low concns. augment it. The phorbol ester tumor promoter, PMA, alone is not mitogenic for primary lymphocytes but enhances the activity of mitogenic lectins. Because the cytochalasans have been reported to increase intracellular Ca2+ and because PMA activates protein kinase C, lymphocytes were treated with PMA and cytochalasin B (CyB) to det. if this combination would induce DNA synthesis. While this treatment by itself did not cause proliferation, lymphocytes cultured with PMA and CyB overnight, washed, and recultured with IL-2 proliferated to the same degree as lymphocytes stimulated with Con A. Three different cytochalasans, cytochalasin B, cytochalasin D, and chaetoglobosin C, all of which bind to cellular actin with different affinities and only one of which affects glucose transport, induced IL-2 receptors in combination with PMA. Flow cytometric anal. with an antibody to the IL-2 receptor .alpha. subunit confirmed the induction of receptors on CD8+ cells. However, no IL-2 was produced after the exposure of lymphocytes to the combination of cytochalasans and PMA. Therefore, there was sufficient signal to induce IL-2 receptor expression but not to induce IL-2.
IT 50645-76-6, Chaetoglobosin C
RL: BIOL (Biological study)
(phorbol ester and, interleukin-1 receptors induction by, on CD8 lymphocyte subset)

L6 ANSWER 45 OF 180 CAPLUS COPYRIGHT 1996 ACS
1992:571215 Document No. 117:171215 Preparation of 3-(heterocyclylmethyl)indoles as drugs. Macor, John Eugene; Wythes, Martin James (Pfizer Inc., USA). PCT Int. Appl. WO 9206973 A1 920430, 82 pp. DESIGNATED STATES: W: AU, BG, BR, CA, CS, DE, FI, HU, JP, KR, NO, PL, RO, SU, US; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, DE, DK, ES, FR, GA, GB, GR, IT, LU, ML, MR, NL, SE, SN, TD, TG. (English). CODEN: PIXXD2. APPLICATION: WO 91-US7194 911008. PRIORITY: US 90-597928 901015.
GI

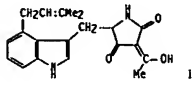


I

AB Title compds. I [n = 0-2; R2 = H, halo, cyano, R4O (wherein R4 = H, C1-6 alkyl, aryl), R6R5NCO(CH2)m, R6R5NSO2(CH2)m (wherein R5, R6 = H, C1-6 alkyl, aryl, C1-3 alkylaryl, R5R6 = 4-6-membered ring), R8CONR7(CH2)m R8SO2NR7(CH2)m (wherein R7, R8 = H, C1-6 alkyl, aryl, C1-3 alkylaryl), R8(O)xS(CH2)m, R6R5NCONR7(CH2)m, R9O2CNR7(CH2)m, R10(CH2)yCH:CH (wherein R9 = H, C1-6 alkyl, aryl, C1-3 alkylaryl, R10 = R6R5NCO, R6R5NSO2, R8CONR7, R8SO2NR7, etc.); m = 0-3; x = 1, 2; y = 0-2; R3 = H, alkyl], useful as 5-HT1 agonists, centrally acting antihypertensives, and vasodilators (no data) are prepd. (R)-3-[N-(Benzyloxycarbonyl)pyrrolidin-2-yl)carbonyl]-5-methoxy-1H-indole (prepn. given) was refluxed with LiAlH4 in THF to give (R)-I (R2 = MeO, R3 = Me, n = 1).
IT 143322-64-9
RL: RCT (Reactant)
(hydrogenation of, in prepn. of serotonin agonist)
IT 143322-46-7P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)
(prepn. and reaction of, in prepn. of indole deriv. drugs)
IT 143321-79-3P 143321-80-6P 143321-81-7P
143321-82-8P 143321-83-9P 143321-84-0P
143322-01-4P 143322-02-5P 143322-03-6P
143322-04-7P 143322-07-0P 143322-57-0P
143322-65-0P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)
(prepn. and reaction of, in prepn. of serotonin agonist)
IT 143321-58-8P 143321-72-6P 143321-73-7P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)
(prepn. and reaction of, in prepn. of serotonin agonist drug)
IT 5275-05-8P 101832-07-9P 143321-54-4P
143321-55-5P 143321-56-6P 143321-57-7P
143321-59-9P 143321-60-2P 143321-61-3P
143321-62-4P 143321-63-5P 143321-74-8P
143321-75-9P 143321-76-0P 143321-77-1P
143321-78-2P 143322-05-8P 143322-06-9P
143322-10-5P 143322-11-6P 143322-12-7P

L6 ANSWER 45 OF 180 CAPLUS COPYRIGHT 1996 ACS (Continued)
143322-13-8P 143322-14-9P 143322-15-0P
143322-16-1P 143322-17-2P 143322-18-3P
143322-19-4P 143322-20-7P 143322-21-8P
143322-22-9P 143322-23-0P 143322-24-1P
143322-25-2P 143322-26-3P 143322-27-4P
143322-28-5P 143322-29-6P 143322-30-9P
143322-31-0P 143322-32-1P 143322-33-2P
143322-34-3P 143322-35-4P 143322-36-5P
143322-37-6P 143322-38-7P 143322-39-8P
143322-40-1P 143322-41-2P 143322-42-3P
143322-43-4P 143322-44-5P 143322-45-6P
143322-47-8P 143322-48-9P 143322-49-0P
143322-50-3P 143322-51-4P 143322-52-5P
143322-53-6P 143322-54-7P 143322-55-8P
143322-58-1P 143322-59-2P 143322-60-5P
143322-61-6P 143322-62-7P 143322-63-8P
143322-67-2P 143322-68-3P 143322-69-4P
143322-71-8P 143393-07-1P 143393-09-3P
143577-59-7P 143577-60-0P 143577-61-1P
143577-63-3P
RL: BAC (Biological activity or effector, except adverse); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of, as drug)

L6 ANSWER 46 OF 180 CAPLUS COPYRIGHT 1996 ACS
1992:448167 Document No. 117:48167 The synthesis of optically pure .beta.-cyclopiazonic acid, an indolic fungal metabolite. Holzapfel, Cedric W.; Kruger, Friedrich W. H. (Dep. Chem. Biochem., Rand Afrikaans Univ., Johannesburg, 2000, S. Afr.). Aust. J. Chem., 45(1), 99-107 (English) 1992. CODEN: AJCHAS. ISSN: 0004-9425.
GI



I

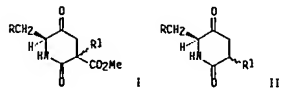
AB The chiral synthesis of the fungal metabolite .beta.-cyclopiazonic acid I is described. The key step involves the use of the tricarbonylchromium complex of an N-protected L-tryptophan Me ester as a substrate for the addn./oxidn. method of substitution of its indole ring system.
IT 142287-59-0P
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of, as cyclopiazonic acid precursor)

L6 ANSWER 47 OF 180 CAPLUS COPYRIGHT 1996 ACS
1992:426178 Document No. 117:26178 Synthesis and Pictet-Spengler reaction of 2-skatylpiperidine, -homopiperidine and -amino acids. Hamama, W. S.; Hammouda, M.; Kandeel, E. M.; Afsah, E. M. (Fac. Sci., Mansoura Univ., Mansoura, Egypt). Zhonghua Yaoxue Zazhi, 44(1), 25-9 (English) 1992. CODEN: CYHCEX. ISSN: 1016-1015.
GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB Schmidt reaction of 2-skatylcycloalkanones I (n = 1, 2) gave the corresponding cyclolactams, which were reduced to the 2-skatylpiperidine (II, n = 1) and -homopiperidine (II, n = 2) resp. Acid hydrolysis of the lactams gave skatylamino acids III (n = 3, 4). Carbolines IV and V were obtained via treatment of III and II with formalin.
IT 5275-05-8P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)
(prepn. and reaction of, with formaldehyde)
IT 141647-89-4P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)
(prepn. and redn. of)

L6 ANSWER 48 OF 180 CAPLUS COPYRIGHT 1996 ACS
1992:256027 Document No. 116:256027 Synthesis of cyclic ketomethylene dipeptide derivatives. Dominguez, M. J.; Gonzalez-Muniz, R.; Garcia-Lopez, M. T. (Inst. Quim. Med., Madrid, 28006, Spain). Tetrahedron, 48(13), 2761-72 (English) 1992. CODEN: TETRAB. ISSN: 0040-4020. OTHER SOURCES: CASREACT 116:256027.
GI

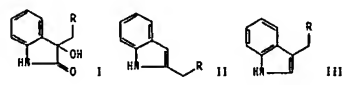


I II

AB Me 6-aralkyl-2,5-diketopiperidine-3-carboxylates I (R = Ph, 3-indolyl; R1 = H) derived from L-Phe and L-Trp, and their 3-substituted analogs I (R = Ph, 3-indolyl; R1 = CH2Ph, CO2CO2Et, Me) in which the 3-substituent is the side chain of Phe, Asp, and Ala have been synthesized. Cyclo[Trp.psi.(COCH2)Gly] (II; R = 3-indolyl, R1 = H) and cyclo[Phe.psi.(COCH2)-.xi.-Phe] (II; R = Ph, R1 = CH2Ph) have been also prepd.
IT 135941-69-4 135941-72-9
RL: RCT (Reactant)
(deprotonation-alkylation reactions or sapon. of)
IT 141672-21-1P 141672-24-4P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)
(prepn. and decarboxylation of)
IT 136969-62-5P 136969-63-6P 136969-66-9P
136969-67-0P 136969-70-5P 136969-71-6P
136969-73-8P
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of)

L6 ANSWER 49 OF 180 CAPLUS COPYRIGHT 1996 ACS
1992:235273 Document No. 116:235273 Contribution of synthetic chemistry for new bioscience. Possibility of biological Diels-Alder reaction. Ichihara, Akitami (Fac. Agric., Hokkaido Univ., Sapporo, 060, Japan). Yuki Gosei Kagaku Kyokaishi, 50(2), 96-111 (Japanese) 1992. CODEN: YGKKAE. ISSN: 0037-9980.
AB A review with 33 refs. on biosynthesis and chem. synthesis of solanapyrones, diplodiatoxin, betaenones, and chaetoglobosin A to study the possibility of biol. Diels-Alder reactions.
IT 50335-03-0P, Chaetoglobosin A
RL: PREP (Preparation)
(biol. and chem. synthesis of, study of Diels-Alder reaction in)

L6 ANSWER 50 OF 180 CAPLUS COPYRIGHT 1996 ACS
1992:59142 Document No. 116:59142 Chemistry of indoles carrying basic functions. I. Transformation of hydroxyindolones into indoles. Moldvai, Istvan; Gacs-Baitz, Eszter; Szantay, Csaba (Cent. Res. Inst. Chem., Hung. Acad. Sci., Budapest, H-1525, Hung.). Recl. Trav. Chim. Pays-Bas, 110(11), 437-40 (English) 1991. CODEN: RTCPA3. ISSN: 0165-0513.
GI



AB 3-Hydroxy-3-(pyridylmethyl)indolones I (R = 2-, 4-pyridyl) have been reduced with NaBH4/MeOH/tert-BuOH. After acidic treatment, 2- and 3-substituted indoles II and III were obtained. The intermediates of the rearrangement were isolated and the effect of the pyridylmethyl groups on the rearrangement has also been established.
IT 5580-44-9P
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of)

L7 21 SEA FILE=CAPLUS L6 AND (5HT1 OR 5(1W)HT1 OR MIGRANE# OR HEADACHE# OR VASODILATOR# OR HYPERTENSION OR ANTIHYPERTENSIVE OR VASOCONSTRICTOR OR RAYMOND?)/AB,BI

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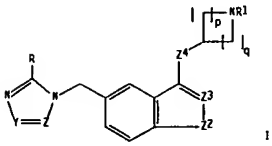
L7 ANSWER 1 OF 21 CAPLUS COPYRIGHT 1996 ACS
1995:987946 Preparation of [(triazolyl)indolyl]methylpyrrolidines as 5-HT1-like agonists.. Matassa, Victor Giulio; Sternfeld, Francine; Street, Leslie Joseph (Merck Sharp and Dohme Ltd., UK). PCT Int. Appl. WO 9521167 A1 950810, 22 pp. DESIGNATED STATES: W: AM, AT, AU, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, JP, KE, KG, KP, KR, KZ, LK, LR, LT, LU, LV, MD, MG, MN, MW, MX, NL, NO, NZ, PL, PT, RO, RU, SD, SE, SI, SK, TJ, TT, UA, US; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, DE, DK, ES, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG. (English). CODEN: PIXXD2. APPLICATION: WO 95-GB135 950124. PRIORITY: GB 94-2011 940202.
AB Title compds. (I; R = H, C1-6 alkyl), were prepd. Thus, 4'-(1,2,4-triazol-4-yl)phenylhydrazine and (2S)-N-tert-butoxycarbonyl-3-(pyrrolidin-2-yl)propanal were stirred in 4% aq. H2SO4 at room temp.-reflux to give 34% I (R = H), isolated as the oxalate. I showed pEC50 .gtoreq.5.0 in a test of their ability to mediate contraction of the saphenous vein of rabbits.
IT RN LIST MAY NOT BE COMPLETE: 154594-16-8 171550-13-3
171550-14-4 171550-15-5 171550-16-6
171752-92-4

L7 ANSWER 2 OF 21 CAPLUS COPYRIGHT 1996 ACS (Continued)
(prepn. of triazole derivs. as serotoninergic agonists)
IT 171182-32-4P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)
(prepn. of triazole derivs. as serotoninergic agonists)

L7 ANSWER 2 OF 21 CAPLUS COPYRIGHT 1996 ACS
1995:969448 Document No. 124:8823 Preparation of triazole derivatives as serotoninergic agonists. Matassa, Victor Giulio; Sternfeld, Francine; Street, Leslie Joseph (Merck Sharp and Dohme Ltd., UK). PCT Int. Appl. WO 9521166 A1 950810, 49 pp. DESIGNATED STATES: W: AM, AT, AU, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, JP, KE, KG, KP, KR, KZ, LK, LR, LT, LU, LV, MD, MG, MN, MW, MX, NL, NO, NZ, PL, PT, RO, RU, SD, SE, SI, SK, TJ, TT, UA, US; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, DE, DK, ES, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG. (English). CODEN: PIXXD2. APPLICATION: WO 95-GB134 950124. PRIORITY: GB 94-2016 940202.
GI



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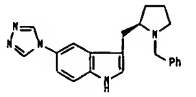


II

AB Title compds. [I; R = H, hydrocarbyl, heterocyclyl, etc.; R1 = cycloalkyl, alkoxyalkyl, aryl(alkyl), etc.; 1 of Y,Z = N and the other = (un)substituted CH; Z1 = bond, alkylene; Z2 = O, S, (alkyl)imino; Z3 = N, (alkyl-substituted)CH; Z4 = alkylene; p = 0 or 1; q = 1-4; p+q = 2-4], agonists of 5-HT1-like receptors, were prepd. Thus, (2R)-N-tert-butoxycarbonylpyrrolidine-2-propanal was cyclocondensed with 4-(1,2,4-triazol-4-yl)phenylhydrazine (prepn. each given) and the product condensed with PhCHO to give title compd. II. I had pEC50 of .gtoreq.5.0 for contraction of rabbit saphenous vein.
IT 171182-20-0P 171182-21-1P 171182-22-2P
171182-23-3P 171182-24-4P 171182-25-5P
171182-26-6P 171182-27-7P 171182-28-8P
171182-29-9P 171182-30-2P 171182-31-3P
RL: BAC (Biological activity or effector, except adverse); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

L7 ANSWER 3 OF 21 CAPLUS COPYRIGHT 1996 ACS
1995:933846 Document No. 124:688 The in vivo pharmacological profile of a 5-HT1 receptor agonist, CP-122,288, a selective inhibitor of neurogenic inflammation. Gupta, P.; Brown, D.; Butler, P.; Ellis, P.; Grayson, K. L.; Land, G. C.; Macor, J. E.; Robson, S. F.; Wythes, M. J.; Shepperson, N. B. (Departments of Discovery Biology and Discovery Chemistry, Pfizer Central Research, Sandwich, Kent, CT13 9NJ, UK). Br. J. Pharmacol., 116(5), 2385-90 (English) 1995. CODEN: BJPCBM. ISSN: 0007-1188.
AB The aim of the present study was to investigate the in vivo pharmacol. profile of CP-122,288, an indole-deriv. with a conformationally restricted N-methylpyrrolidinyl basic side chain in the C-3 position. This C-3 substituent structurally differentiates CP-122,288 from the 5-HT1D receptor agonist sumatriptan, which possesses an N,N-dimethylaminoethyl group. When administered prior to elec. stimulation of the trigeminal ganglion, CP-122,288 (0.3-300 ng kg-1, i.v.) produced a dose-related inhibition of plasma protein extravasation in rat dura mater (min. ED, MED, 3 ng kg-1 i.v., P < 0.05; maximal inhibition of plasma extravasation at 30 ng kg-1 i.v., P < 0.01). Sumatriptan produced a similar inhibition of plasma leakage in the dura, but at much higher dose levels (MED, 100 .mu.g kg-1 i.v., P < 0.05). Thus, CP-122,288 is of the order of 104 fold more potent than sumatriptan. At all doses tested, CP-122,288 did not inhibit plasma protein extravasation measured in extracranial tissues such as the lower lip, eyelid, and conjunctiva. In a sep. series of studies in the anesthetized rat, CP-122,288 (0.003-3 .mu.g kg-1 i.v.) produced no change in either heart rate or mean arterial blood pressure, thus demonstrating that doses of CP-122,288 which inhibit plasma protein leakage in rat dura, are devoid of hemodynamic effects. Following a 5 min period of elec. stimulation of the trigeminal ganglion, a 20 min period of sustained neurogenically-driven plasma extravasation, occurring in the absence of elec. stimulation, was initiated. By administration of the compd. 5 min after completing the phase of elec. stimulation, this protocol permitted the evaluation of the activity of CP-122,288 on the ongoing and established inflammatory event. CP-122,288 (30 and 300 ng kg-1, i.v. P <0.01 and P <0.05, resp.) produced a complete inhibition of plasma protein leakage which was consistent with its effects when administered prior to trigeminal ganglion stimulation. In the anesthetized dog, CP-122,288 and sumatriptan, at 1-300 .mu.g kg-1, i.v., produced a dose-dependent redn. in carotid arterial blood flow and coronary arterial diam. These data demonstrate that sumatriptan inhibits neurogenic inflammation in the rat (MED, 100 .mu.g kg-1, i.v.) and produces vasoconstriction in the dog, over a similar dose-range. Interestingly, doses of CP 122,288 that inhibit neurogenic inflammation in rat dura mater (0.3-300 ng kg-1) were demonstrated to be devoid of vasoconstrictor activity in either the carotid or coronary vascular beds of dog. These data demonstrate that in the rat, CP-122,288 is a highly potent and selective inhibitor of neurogenic inflammation in intracranial tissues, at doses which are devoid of vasoconstrictor activity in dog. Potentially, CP-122,288 may be of use for the acute treatment of migraine, without the risk of cardiovascular side-effects.
IT 143321-74-8, CP-122288
RL: ADV (Adverse effect, including toxicity); BAC (Biological activity or effector, except adverse); THU (Therapeutic use); BIOL

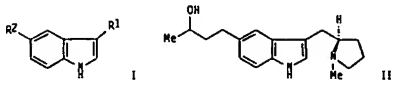
L7 ANSWER 3 OF 21 CAPLUS COPYRIGHT 1996 ACS (Continued)
(Biological study); USES (Uses)
(CP-122,288 pharmacol. profile as selective inhibitor of neurogenic inflammation in relation to migraine treatment)

L7 ANSWER 4 OF 21 CAPLUS COPYRIGHT 1996 ACS (Continued)
167302-93-4P 167302-94-5P 167302-95-6P
167302-96-7P 167302-97-8P 167302-98-9P
167302-99-0P 167303-00-6P 167303-01-7P
167303-02-8P 167303-03-9P 167303-04-0P
167303-05-1P 167303-06-2P 167303-07-3P
167303-08-4P 167303-09-5P 167303-10-8P
167303-11-9P 167303-12-0P 167303-13-1P
167303-14-2P 167303-15-3P 167303-16-4P
167303-17-5P 167303-18-6P 167303-19-7P
167303-20-0P 167303-21-1P 167303-23-3P
167303-24-4P 167303-25-5P 167303-26-6P
167303-27-7P 167303-28-8P 167303-29-9P
167303-30-2P 167303-31-3P
RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of (pyrrolidinylmethyl)indoles 5-HT1 -like agonists)

L7 ANSWER 4 OF 21 CAPLUS COPYRIGHT 1996 ACS

1995:772570 Document No. 123:169499 Indole derivatives as 5-HT1-like agonists for use in migraine. Wythes, Martin James (Pfizer Ltd., UK; Pfizer Inc.; Pfizer Research and Development Company, N.V./S.A.). PCT Int. Appl. WO 9424127 A1 941027, 124 pp. DESIGNATED STATES: W: AU, BR, CA, CN, CZ, FI, HU, JP, KR, NO, NZ, PL, RU, US; RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE. (English). CODEN: PIXXD2. APPLICATION: WO 94-EP1121 940411. PRIORITY: GB 93-8360 930422; GB 93-24433 931127.

GI



AB The title compds., 3-(pyrrolidinylmethyl)indoles and 3-(piperidinylmethyl)indoles I [R1 = (2-pyrrolidinyl)methyl, 3-pyrrolidinyl, 4-piperidinyl, (3-piperidinyl)methyl; R2 = alkyl, oxoalkyl, etc.] were disclosed as selective 5-HT1 -like agonists useful in the treatment of migraine, cluster headache, chronic paroxysmal hemicrania and headache assocd. with vascular disorders. A specifically claimed example compd. is 5-(3-hydroxybutyl)-3-[(R)-(1-methyl-2-pyrrolidinyl)methyl]-1-H-indole (II).

IT 143322-57-0
RL: RCT (Reactant)
(prepn. of (pyrrolidinylmethyl)indoles 5-HT1 -like agonists)

IT 143322-46-7P 153435-71-3P 153435-73-5P
153525-35-0P 153525-50-9P 153525-51-0P
167303-50-6P 167303-51-7P 167303-54-0P
167303-55-1P 167303-56-2P 167303-63-1P
167303-64-2P 167303-66-4P 167303-67-5P
167303-71-1P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)
(prepn. of (pyrrolidinylmethyl)indoles 5-HT1 -like agonists)

IT 167302-44-5P 167302-45-6P 167302-46-7P
167302-47-8P 167302-48-9P 167302-49-0P
167302-50-3P 167302-51-4P 167302-52-5P
167302-53-6P 167302-54-7P 167302-55-8P
167302-56-9P 167302-62-7P 167302-63-8P
167302-64-9P 167302-65-0P 167302-66-1P
167302-71-8P 167302-72-9P 167302-73-0P
167302-74-1P 167302-75-2P 167302-76-3P
167302-77-4P 167302-78-5P 167302-79-6P
167302-80-9P 167302-81-0P 167302-82-1P
167302-83-2P 167302-84-3P 167302-92-3P

L7 ANSWER 5 OF 21 CAPLUS COPYRIGHT 1996 ACS

1995:549880 Document No. 122:306133 Effect of a 5-HT1 receptor agonist, CP-122,288, on edema formation induced by stimulation of the rat saphenous nerve. Kajekar, Radhika; Gupta, Paul; Shepperson, Nicholas B.; Brain, Susan D. (Vascular Biology Research Centre, King's College, London, SW3 6LX, UK). Br. J. Pharmacol., 115(1), 1-2 (English) 1995. CODEN: BJPCBM. ISSN: 0007-1188.

AB Neurogenic edema formation in the rat hind paw skin induced by elec. stimulation of the saphenous nerve and measured by extravasation of [125I]-albumin, was inhibited by the 5-HT1B receptor agonist, CP-93,129, and the novel tryptamine analog, CP-122,288. Significant inhibition of up to 66% of control was obsd. with CP-122,288 (2 .times. 10-14 - 2 .times. 10-7 mol kg-1) and CP-93,129 (5 .times. 10-7-5 .times. 10-6 mol kg-1), with the min. ED for CP-122,288 being about 107 fold less than that for GP-93,129. Edema formation induced by the intradermal administration of exogenous mediators (substance P and histamine) in rat dorsal skin was not inhibited by CP-122,288 (2 .times. 10-10 mol kg-1). These results suggest that CP-122,288 is a potent inhibitor of neurogenic inflammation in rat skin and that the effect may be due to a prejunctional inhibition of neuropeptide release.

IT 143321-74-8, CP-122288
RL: BAC (Biological activity or effector, except adverse); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(neurogenic edema inhibition by 5-HT1 receptor agonist CP-122288)

L7 ANSWER 6 OF 21 CAPLUS COPYRIGHT 1996 ACS
1995:466381 Document No. 122:256183 The pre- and postjunctional activity of CP-122,288, a conformationally restricted analog of sumatriptan. Beattie, David T.; Connor, Helen E. (Pharmacology II, Glaxo Research and Development Ltd., Park Road, Ware Herts, SG12 0DP, UK). Eur. J. Pharmacol., 276(3), 271-6 (English) 1995. CODEN: EJPHAZ. ISSN: 0014-2999.

AB The present study investigated the pre- and postjunctional activity of CP-122,288 (5-methyl-aminosulfonylmethyl-3-(N-methylpyrrolidin-2R-yl-methyl)-1H -indole), an analog of the vascular 5-HT1 receptor agonist, sumatriptan. CP-122,288 inhibited neurogenic plasma protein extravasation in rat dura with a potency approx. 40 000-fold greater than sumatriptan (ID50 values of 0.3 pmol/kg and 13.9 nmol/kg i.v. resp.). However, CP-122,288 was only approx. 2-fold more potent than sumatriptan at inhibiting neurogenically mediated contractions of the dog saphenous vein. CP-122,288 contracted the dog saphenous vein and basilar artery with a potency approx. 2-fold greater than that of sumatriptan. Both compds. possessed similar affinities at either human 5-HT1D.alpha. or 5-HT1D.beta. receptors. It is concluded that CP-122,288 exhibits a prejunctional selectivity in the meninges to inhibit dural plasma protein extravasation independent of 5-HT1D.alpha. and 5-HT1D.beta. receptor activation.

IT 143321-74-8, CP-122288
RL: BAC (Biological activity or effector, except adverse); BIOL (Biological study)
(pre- and postjunctional activity of CP-122,288, a conformationally restricted analog of sumatriptan)

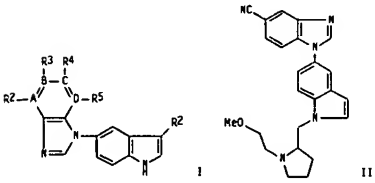
L7 ANSWER 7 OF 21 CAPLUS COPYRIGHT 1996 ACS
1995:421524 Document No. 122:205025 Suppression by the sumatriptan analog, CP-122,288 of c-fos immunoreactivity in trigeminal nucleus caudalis induced by intracisternal capsaicin. Cutrer, F. Michael; Schoenfeld, David; Limmroth, Volker; Panahian, Nariman; Moskowitz, Michael A. (Harvard Med. Sch., Massachusetts Gen. Hosp., Boston, MA, 02114, USA). Br. J. Pharmacol., 114(5), 987-92 (English) 1995. CODEN: BJPCBM. ISSN: 0007-1188.

AB The effects of an i.v. administered sumatriptan analog were exmd. on c-fos-like immunoreactivity (c-fos-LI), a marker of neuronal activation, evoked within trigeminal nucleus caudalis (TNC) and other brain stem regions 2 h after intracisternal injection of the irritant, capsaicin (0.1 nn, 0.3 nM), in pentobarbitone-anesthetized Hartley guinea pigs. C-fos-LI was assessed in eighteen serial sections (50 .mu.m) using a polyclonal antiserum. A weighted av., reflecting total expression within lamina I, IIO of TNC was obtained from three representative levels (i.e., at -0.225 mm, -2.475 mm and -6.075 mm). Capsaicin caused significant labeling within lamina I, IIO, a region contg. axonal terminatns of small unmyelinated C-fibers, as well as within the nucleus of the solitary tract, area postrema and medial reticular nucleus. A similar distribution of pos. cells was reported previously after intracisternal injection of other chem. irritants such as autologous blood or carrageenin. Pretreatment with a conformationally restricted sumatriptan analog (with some selectivity for 5-HT1B and 5-HT1D receptor subtypes) CP-122,288, reduced the weighted av. by approx. 50-60% ($P < 0.05$) in lamina I, IIO at 100 pmol kg-1, i.v., but did not decrease cell no. within area postrema, nucleus of the solitary tract or medical reticular nucleus. A similar pattern was reported previously following sumatriptan, dihydroergotamine or CP-93,129 administration after noxious meningeal stimulation. We conclude that modifications at the amino-Et side chain of sumatriptan dramatically enhance the suppression of c-fos expression within TNC, a finding consistent with its remarkable potency against neurogenic plasma protein extravasation within dura matter. CP-122,288 and related analogs may serve as an important prototype for drug development in migraine and related headaches.

IT 143321-74-8, CP-122288
RL: BAC (Biological activity or effector, except adverse); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(suppression by sumatriptan analog, CP-122,288 of c-fos immunoreactivity in trigeminal nucleus caudalis induced by intracisternal capsaicin)

L7 ANSWER 8 OF 21 CAPLUS COPYRIGHT 1996 ACS
1995:354225 Document No. 122:133200 5-arylindole derivatives and their use as serotonin (5-HT1) agonists. Macor, John Eugene (Pfizer Inc., USA). PCT Int. Appl. WO 9410171 A1 940511, 72 pp. DESIGNATED STATES: W: AU, BR, CA, CZ, JP, KR, NO, NZ, PL, RU, US; RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE. (English). CODEN: PIXXD2. APPLICATION: WO 93-US9790 931019. PRIORITY: US 92-970758 921102.

GI


I

II

AB The title compds. I (R1 = aminoalkyl; R2-R5 = H, alkyl, aryl, etc.) were disclosed. I are useful in treating migraine and other disorders; they are useful psychotherapeutics and are potent serotonin (5-HT1) agonists and benzodiazepine agonists and antagonists and may be used in the treatment of depression, anxiety, eating disorders, obesity, drug abuse, cluster headache, migraine, pain and chronic paroxysmal hemicrania and headache assocd. with vascular disorders, and other disorders arising from deficient serotonergic neurotransmission. I are also useful as centrally acting antihypertensives and vasodilators. A specifically claimed example compd. is 5-cyano-1-[[3-[1-(2-methoxyethyl)-2-pyrrolidinyl]methyl]-5-indolyl]-1H-benzimidazole (II).

IT 160907-04-0P 160907-05-1P 160907-06-2P
160907-07-3P
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of)

IT 143322-01-4P 151272-89-8P 151272-90-1P
151272-99-0P 151273-00-6P 151273-01-7P
151273-05-1P 151273-06-2P 151273-07-3P
151273-08-4P 151273-11-9P 158752-53-5P
160906-44-5P 160906-45-6P 160906-46-7P
160906-47-8P 160906-48-9P 160906-49-0P
160906-50-3P 160906-51-4P 160906-54-7P
160906-55-8P 160906-81-0P 160906-82-1P
160906-83-2P 160906-84-3P 160906-85-4P
160906-86-5P 160906-87-6P 160906-95-6P
160906-96-7P 160906-97-8P 160907-00-6P
160907-08-4P

L7 ANSWER 8 OF 21 CAPLUS COPYRIGHT 1996 ACS (Continued)
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of, as intermediate for arylindole serotoninergic agonist)

IT 160906-56-9P 160906-57-0P 160906-58-1P
160906-59-2P 160906-60-5P 160906-61-6P
160906-62-7P 160906-63-8P 160906-64-9P
160906-65-0P 160906-66-1P 160906-68-3P
160906-69-4P 160906-72-9P 160906-73-0P
160906-74-1P 160906-75-2P 160906-79-6P
160906-80-9P 160906-91-2P 160906-94-5P
160907-03-9P
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of, as serotoninergic agonist)

IT 151272-88-7
RL: RCT (Reactant)
(reactant for arylindole serotoninergic agonist)

IT 160907-09-5
RL: RCT (Reactant)
(serotoninergic agonist)

L7 ANSWER 9 OF 21 CAPLUS COPYRIGHT 1996 ACS
1995:300051 Document No. 122:64328 Use of indole derivatives as 5-HT1 antagonists. Macor, John Eugene (Pfizer Inc., USA). PCT Int. Appl. WO 9425023 A1 941110, 22 pp. DESIGNATED STATES: W: AU, BG, BR, CA, CN, CZ, FI, HU, JP, KR, NO, NZ, PL, RO, RU, SK; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, DE, DK, ES, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG. (English). CODEN: PIXXD2. APPLICATION: WO 94-IB79 940426. PRIORITY: US 93-53930 930427.

AB The present invention relates to pharmaceutical compns. contg. (R)-5-(methylaminosulfonylmethyl)-3-(N-methylpyrrolidin-2-ylmethyl)-1H-indole or (R)-5-(methylaminosulfonylmethyl)-3-(pyrrolidin-2-ylmethyl)-1H-indole for the treatment of conditions such as hypertension, depression, anxiety, eating disorders, obesity, drug abuse, cluster headache, migraine, pain, chronic paroxysmal hemicrania, and headache assocd. with vascular disorders.

IT 143321-82-8P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)
(indole derivs. for treatment of disorders from deficient serotonergic neurotransmission)

IT 143321-74-8P 143321-78-2P
RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(indole derivs. for treatment of disorders from deficient serotonergic neurotransmission)

L7 ANSWER 10 OF 21 CAPLUS COPYRIGHT 1996 ACS
1994:483048 Document No. 121:83048 (Acylamino)indole derivatives as 5-HT1 agonists. Macor, John E. (Pfizer Inc., USA). PCT Int. Appl. WO 9321180 A1 931028, 32 pp. DESIGNATED STATES: W: AU, BR, CA, CZ, DE, JP, KR, NO, NZ, PL, RU, SK, UA, US; RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE. (English). CODEN: PIXXD2. APPLICATION: WO 93-US1807 930304. PRIORITY: US 92-866382 920410.

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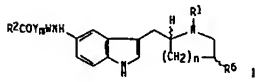


I

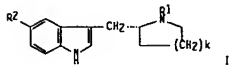
AB The title compds. I [R1 = H, C1-6 alkyl, C3-6 alkenyl, C3-6 alkynyl, (un)substituted aryl, etc.; R2 = CF3, C1-6 alkyl, aryl, C1-3 alkylaryl, etc.; R6 = H, OH, alkoxy, aryloxy, acylamino, etc.; W, Y = amino acid residue; m = 0, 1; n = 0-2], which are 5-HT1 agonists (no data), useful in the treatment of hypertension (no data), depression (no data), anxiety (no data), pain (no data), etc., are prepd. Thus, N-benzyloxycabonylglycine was coupled with 5-amino-3-(N-methylpyrrolidin-2R-ylmethyl)-1H-indole, producing 5-(N-benzyloxycarbonylglycyl)amino-3-(N-methylpyrrolidin-2R-ylmethyl)-1H-indole in 74% yield.

IT 143321-58-8 143322-01-4 151272-89-8
154038-83-2 154038-84-3 154038-85-4
154038-86-5
RL: RCT (Reactant)
(prepn. as serotoninergic receptor agonist)

IT 143321-58-8 143322-01-4 151273-38-0
RL: RCT (Reactant)
(reactant, in prepn. of (acylamino)indole serotoninergic receptor agonists)

L7 ANSWER 11 OF 21 CAPLUS COPYRIGHT 1996 ACS
1994:457330 Document No. 121:57330 Preparation of indole derivatives as 5-HT1-like agonists. Macor, John Eugene; Wythes, Martin James (Pfizer Ltd., UK; Pfizer Inc.; Pfizer Research and Development Co., N.V./S.A.). PCT Int. Appl. WO 9321177 A1 931028, 70 pp. DESIGNATED STATES: W: AU, BR, CA, CZ, FI, HU, JP, KR, NO, NZ, PL, RU, SK, UA, US; RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE. (English). CODEN: PIXXD2. APPLICATION: WO 93-EP738 930325. PRIORITY: GB 92-7930 920410.

GI



I

AB Title compds. I [R1 = (C1-6 acyl)-C1-3 alkylene, (C1-6 alkyl-O2C)-C1-3 alkylene, (H2NOC)-C1-3 alkylene, (H2NO2S)-C1-3 alkylene, (HO) C3-7 cycloalkyl, (aryl) C3-6 alkenyl, heteroaryl-C1-3 alkylene etc.; R2 = H, halo, F3C, NC, H2NOC, HO, etc.; k = 0-2] or a salt thereof, are prepd. 5-(2-Ethylsulfonylethyl)-3-(2R-pyrrodinylmethyl)-1H-indole (prepn. given) was reacted with 2-pyridylmethyl chloride to give I (R1 = 2-pyridylmethyl, R2 = 2-EtSO2CH2CH2, k = 1). A similar prepd. I (R1 = EtCOCH2, R2 = EtSO2CH2CH2, k = 1) evaluated for max. contraction on saphenous vein strip showed an EC50 = 3.1 .times. 10-3M.

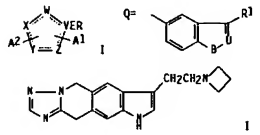
IT 143322-48-9P 153435-71-3P 153525-51-0P
153525-52-1P 153525-53-2P 153525-54-3P
153525-55-4P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)
(prepn. and reaction of, prepn. of 5-HT1 agonists)

IT 143322-46-7P 143322-47-8P 153525-57-6P
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of)

IT 153435-72-4P 153435-73-5P 153525-10-1P
153525-11-2P 153525-12-3P 153525-13-4P
153525-14-5P 153525-15-6P 153525-16-7P
153525-17-8P 153525-18-9P 153525-19-0P
153525-20-3P 153525-21-4P 153525-22-5P
153525-23-6P 153525-24-7P 153525-25-8P
153525-26-9P 153525-27-0P 153525-28-1P
153525-29-2P 153525-30-5P 153525-31-6P
153525-32-7P 153525-33-8P 153525-34-9P
153525-35-0P 153525-36-1P 153525-37-2P
153525-38-3P 153525-39-4P 153525-40-7P
153525-41-8P 153525-42-9P 153525-43-0P
153525-44-1P 153525-45-2P 153525-46-3P
153525-47-4P 153525-48-5P 153525-49-6P
153525-50-9P
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of, as 5HT1 agonist)

L7 ANSWER 12 OF 21 CAPLUS COPYRIGHT 1996 ACS
1994:298634 Document No. 120:298634 Preparation of imidazole, triazole, and tetrazole derivatives as 5-HT1 -like receptor agonists. Castro Pineiro, Jose Luis; Castro, Pineiro Jose Luis; Guiblin, Alexander Richard; Matassa, Victor Giulio; Reeve, Austin John; Sternfeld, Francine; Street, Leslie Joseph (Merck Sharp and Dohme Ltd., UK). PCT Int. Appl. WO 9402477 A1 940203, 83 pp. DESIGNATED STATES: W: AU, CA, JP, US; RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE. (English). CODEN: PIXXD2. APPLICATION: WO 93-GB1495 930715. PRIORITY: GB 92-15721 920724; GB 92-25657 921208.

GI



I

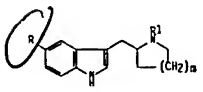
AB Title compds. [I; the broken circle represents two non-adjacent double bonds in any position in the five-membered ring; A1 = H, hydrocarbyl, heterocyclyl, halo, etc.; A2 = groups cited for A1, etc.; E = bond, alkylene; R = heteroaryl group Q; B = O, S, NR3; R1 = 2-pyrrolidinoethyl, 3-aminocyclobutyl, 3-pyrrolidinylmethyl, etc.; U = N, CR2; R2,R3 = H, alkyl; 2-4 of V,W,X,Y,Z = N and the other(s) = C (s1c)] were prepd. Thus, 1-(4-hydrazinophenyl)methyl-1,2,4-triazole and 4-(3-azetidinyl)butanal di-Me acetal (prepn. each given) were subjected to Fischer indole synthesis conditions to give title compd. II. I had pEC50 of .gtoreq.5.0 for mediation of rabbit saphenous vein contraction.

IT 154748-38-6P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)
(prepn. and reaction of, in prepn. of 5-HT1 -like receptor agonist)

IT 154748-36-4P 154748-37-5P 154748-39-7P
154804-04-3P
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of, as 5-HT1-like receptor agonist)

L7 ANSWER 13 OF 21 CAPLUS COPYRIGHT 1996 ACS
1994:217271 Document No. 120:217271 Indole derivatives as 5-HT1 agonists. Brown, Alan Daniel; Dickinson, Roger Peter; Wythes, Martin James (Pfizer Ltd., UK; Pfizer Inc.; Pfizer Research and Development Co., N.V./S.A.). PCT Int. Appl. WO 9321178 A1 931028, 146 pp. DESIGNATED STATES: W: AU, BR, CA, CZ, FI, HU, JP, KR, NO, NZ, PL, RU, SK, UA, US; RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE. (English). CODEN: PIXXD2. APPLICATION: WO 93-EP867 930408. PRIORITY: GB 92-8161 920414.

GI



I

AB The title compds. I [R = (un)substituted Ph, pyridinyl, pyridazinyl, pyrimidinyl, pyrazinyl, furyl, thienyl; R1 = H, C1-6 alkyl, C3-7 cycloalkyl, C5-7 cycloalkenyl, C3-6 alkenyl, C3-6 alkynyl, etc.; m = 1, 2], which are selective agonists at the 5-HT1 -like subtype of the 5-hydroxytryptamine receptor, are prepd. Thus, I (R = 3-C6H4SO2NH2, R1 = Me, m = 1) was prepd. and demonstrated 50% max. contraction of dog-isolated saphenous vein strip at 3.78 X 10-9 M.

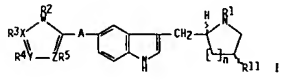
IT 153434-62-9 153434-63-0 153434-64-1
153434-65-2 153434-66-3 153434-67-4
153434-68-5 153434-69-6 153434-70-9
153434-71-0 153434-72-1 153434-73-2
153434-74-3 153434-75-4 153434-76-5
153434-77-6 153434-78-7 153434-79-8
153434-80-1 153434-81-2 153434-82-3
153434-83-4 153434-84-5 153434-85-6
153434-86-7 153434-87-8 153434-88-9
153434-89-0 153434-90-3 153434-91-4
153434-92-5 153434-93-6 153434-94-7
153434-95-8 153434-96-9 153434-97-0
153434-98-1 153434-99-2 153435-00-8
153435-01-9 153435-02-0 153435-03-1
153435-04-2 153435-05-3 153435-06-4
153435-07-5 153435-08-6 153435-09-7
153435-10-0 153435-11-1 153435-12-2
153435-13-3 153435-14-4 153435-15-5
153435-16-6 153435-17-7 153435-18-8
153435-19-9 153435-20-2 153435-21-3
153435-22-4 153435-23-5 153435-24-6
153435-25-7 153435-26-8
RL: RCT (Reactant)
(prepn. as 5-HT1 receptor agonist)

IT 143322-46-7 143322-57-0 153435-54-2
153435-55-3 153435-56-4 153435-57-5

L7 ANSWER 13 OF 21 CAPLUS COPYRIGHT 1996 ACS (Continued)
153435-58-6 153435-71-3 153435-72-4
153435-73-5
RL: RCT (Reactant)
(prepn. as intermediate in prepn. of 5-HT1 receptor agonists)

L7 ANSWER 14 OF 21 CAPLUS COPYRIGHT 1996 ACS
1994:106995 Document No. 120:106995 Preparation of azole indole derivatives as 5-HT1 agonists. Macor, John E.; Nowakowski, Jolanta T. (Pfizer Inc., USA). PCT Int. Appl. WO 9318032 A1 930916, 38 pp. DESIGNATED STATES: W: AU, BR, CA, CZ, DE, JP, KR, NO, NZ, PL, RU, SK, UA, US; RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE. (English). CODEN: PIXXD2. APPLICATION: WO 93-US1667 930303. PRIORITY: US 92-846640 920305.

GI



I

AB Title compds. I (A = bond, C1-4 alkyl, C1-4 alkenyl; n = 0-2; R1 = H, C1-6 alklaryl, aryl, C1-3 alkylheteroaryl, R6(CH2)m wherein R6 = NC, F3C, etc., m = 1-3; W, X, Y, Z = O, S, N, C such that at least one of W, X, Y, Z is N; R2, R3, R4, R5 = H, O1-6 alkyl, aryl, C1-3 alkylaryl, C1-3 alkylheteroaryl, halo, NC, F3C, O2N, etc.; one of R2R3, R3R4, R4R5 = 5-7-membered alkyl ring, 6-membered alkyl ring, 5-7-membered heteroalkyl having 1 of O, N, S, etc.; R11 = H, R12O, R12OHH wherein R12 = C1-6 alkyl, aryl, C1-3 alkylaryl) an a salt thereof useful as 5-HT, agonists (no data) and in disorders arising from deficient serotoninergic neurotransmission (no data), are prepd. (R)-I (A = bond, n = 1, R1 = PhCH2O2C, W = S, Z = N, X = Y = C, R2 = R3 = R11 = H, R4 = PhCH2) (prepn. given) in THF was treated with LiAlH4 to give (R)-I (A = bond, n = 1, R1 = Me, W = S, Z = N, X = Y = C, R2 = R3 = R11 = H, R4 = PhCH2).

IT 152362-19-1P 152362-20-4P 152362-21-5P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)
(prepn. and reaction of, in prepn. of 5-HT1 agonist)

IT 152362-15-7P 152362-16-8P 152362-17-9P
152362-18-0P 152362-32-8P 152362-33-9P
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of, as 5-HT1 agonist)

L7 ANSWER 15 OF 21 CAPLUS COPYRIGHT 1996 ACS
1994:106761 Document No. 120:106761 Indole derivatives as serotonin receptor (5-HT1) agonists. Macor, John E.; Wythes, Martin J. (Pfizer Inc., USA). PCT Int. Appl. WO 9320073 A1 931014, 43 pp. DESIGNATED STATES: W: AU, BR, CA, CZ, DE, JP, KR, NO, NZ, PL, RU, SK, UA, US; RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE. (English). CODEN: PIXXD2. APPLICATION: WO 93-US1967 930310. PRIORITY: US 92-864737 920407.

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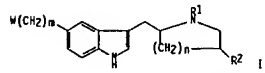

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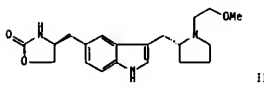


II

AB Three members of claimed indoles I [n = 0-2; m = 0-3; W = 7 types of oxo- and/or thioxo-substituted azolidinyl radicals (pyrrolidinyl, imidazolidinyl, oxazolidinyl, thiazolidinyl) with optional addnl. substitutents; R1 = H, (hydroxy)alkyl, alkenyl, alkynyl, aryl, alkylaryl (sic, e.g., CH2Ph), alkylheteroaryl, certain heterofunctional-terminated alkyl; R2 = H, OR3, NHCOR3; R3 = H, , alkyl, aryl, alkylaryl], potent 5-HT1 agonists (no data), were prepd. for treatment of hypertension, depression, anxiety, obesity, migraine, etc. For example, Mitsunobu coupling of the alc. (R)-1-(N-benzyloxycarbonylpyrrolidin-2-yl)-3-hydroxypropene with 2-bromo-4-(2-oxo-1,3-oxazolidin-4(S)-ylmethyl)-1-(trifluoroacetylamino)benzene at the amide N (100% yield), followed by Pd(OAc)2-catalyzed cyclization to an indole (40%), hydrogenolytic deprotection (89%), and N-alkylation with MeOCH2CH2Br (36%), gave title compd. II.

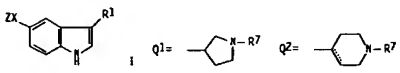
IT 143322-57-0P
RL: SPN (Synthetic preparation); PREP (Preparation)
(Pd-catalyzed coupling; prepn. of indole derivs. as 5-HT1 agonists)

IT 152305-14-1P 152305-19-6P 152305-20-9P
152305-21-0P 152305-24-3P 152305-25-4P
RL: SPN (Synthetic preparation); PREP (Preparation)
(intermediate; prepn. of indole derivs. as 5-HT1 agonists)

IT 152305-12-9P 152305-13-0P 152305-22-1P
152305-26-5P
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of indole derivs. as 5-HT1 agonists)

L7 ANSWER 16 OF 21 CAPLUS COPYRIGHT 1996 ACS
1993:662341 Document No. 119:262341 Conformationally restricted sumatriptan analogs, CP-122,288 and CP-122,638 exhibit enhanced potency against neurogenic inflammation in dura mater. Lee, Won Suk; Moskowitz, Michael A. (Stroke Research Laboratory, Neurosurgery and Neurology Services, Massachusetts General Hospital, Harvard Medical School, 32 Fruit Street, Boston, MA, 02114, USA). Brain Res., 626(1-2), 303-5 (English) 1993. CODEN: BRREAP. ISSN: 0006-8993.
AB CP-122,288 and CP-122,638 (analogs of sumatriptan in which the C3-aminoethyl side chain has been modified) blocked plasma protein extravasation response within dura mater following trigeminal ganglion stimulation. The threshold (1 and 0.1 pmol/kg, resp.) was remarkably lower than for sumatriptan (7 nmol/kg), as was the dose at max. response. As with sumatriptan, substance P-induced plasma leakage was unaffected by either compd., and metergoline only partially (27%) reversed the effects of CP-122,288. The data suggest the importance of modifications at the aminoethyl side chain to the actions of sumatriptan and possibly to the treatment of migraine headache.
IT 143321-74-8, CP 122288 143321-78-2, CP 122638
RL: BIOL (Biological study)
(neurogenic pachymeningitis-inhibition by, structure in relation to)

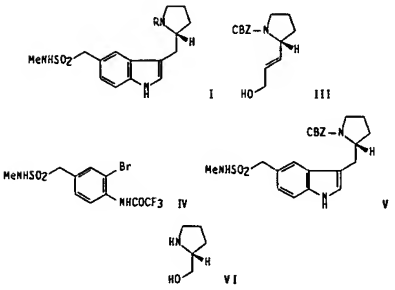
L7 ANSWER 17 OF 21 CAPLUS COPYRIGHT 1996 ACS
1993:649833 Document No. 119:249833 Indole derivatives which are potent serotinin receptor antagonists. Macor, John E. (Pfizer Inc., USA). PCT Int. Appl. WO 9311106 A1 930610, 65 pp. DESIGNATED STATES: W: AU, BR, CA, CS, OE, FI, HU, JP, KR, NO, PL, RU, UA, US; RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, SE. (English). CODEN: PIXXD2. APPLICATION: WO 92-US8306 921006. PRIORITY: US 91-796744 911125.
GI



I

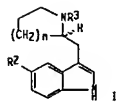
AB The title compds. I [R1 = CH2CH2NR7R8, Q1, Q2 (dotted line represents an optional double bond), etc.; R7,R8 = H, C1-6alkyl, aryl, C1-3alkylaryl, etc.; X = O, NH, S; Z = (un)substituted 5- or 6-membered heterocycleo; R7R8 may form a 4- to 6-membered ring], which are potent serotonin (5-HT1) receptor antagonists (no data), useful in the treatment of hypertension (no data), depression (no data), anxiety (no data), eating disorders (no data), obesity (no data), etc., are prepd. Thus, (R)-5-amino-3-(pyrrolidin-2-ylmethyl)-1-H-indole was prepd. by hydrogenolysis of (R)-3-(N-benzyloxycarbonylpyrrolidin-2-ylmethyl)-5-dibenzylamino-1H-indole.
IT 143321-58-8P 143322-01-4P 151272-88-7P
151272-89-8P 151272-90-1P 151272-99-0P
151273-00-6P 151273-01-7P 151273-02-8P
151273-03-9P 151273-04-0P 151273-05-1P
151273-06-2P 151273-07-3P 151273-08-4P
151273-09-5P 151273-11-9P 151273-12-0P
151273-13-1P 151273-14-2P 151273-15-3P
151273-16-4P 151273-17-5P 151273-18-6P
151273-19-7P 151273-20-0P 151273-21-1P
151273-38-0P 151273-42-6P 151273-44-8P
151273-46-0P 151273-48-2P 151305-77-0P
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. and serotonin receptor antagonist activity of)
IT 143322-68-3 151273-10-8
RL: RCT (Reactant)
(reaction of, in prepn. of indole serotonin receptor antagonist)

L7 ANSWER 18 OF 21 CAPLUS COPYRIGHT 1996 ACS
1993:168927 Document No. 118:168927 Synthesis of a conformationally restricted analog of the anti-migraine drug sumatriptan. Macor, John E.; Blank, David H.; Post, Ronald J.; Ryan, Kevin (Cent. Res. Div., Pfizer Inc., Groton, CT, 06340, USA). Tetrahedron Lett., 33(52), 8011-14 (English) 1992. CODEN: TELEAY. ISSN: 0040-4039. OTHER SOURCES: CASREACT 118:168927.
GI



AB The synthesis of conformationally restricted sumatriptan analog I (R = Me) (II) is described. The Mitsunobu coupling of hydroxypropene III (CBZ = benzyloxycarbonyl) with trifluoroacetanilide IV in the presence of Ph3P and DEAD gave 67% intermediate V, which underwent an intramol. Heck reaction with Pd(OAc)2 in the presence of Et3N in DMF to give 81% protected analog I (R = CBZ). A bonus of the latter cyclization was the concomitant loss of the trifluoroacetyl group. I (R = CBZ) was reduced with LiAlH4 in refluxing THF gave 65% II. III was prepd. from pyrrolidine VI in 4 steps, whereas IV was prepd. from 4-O2NC6H4CH2Cl in 6 steps.
IT 143321-74-8P
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. and antimigraine activity of)
IT 143321-82-8P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)
(prepn. and hydride redn. of)

L7 ANSWER 19 OF 21 CAPLUS COPYRIGHT 1996 ACS
1992:571215 Document No. 117:171215 Preparation of 3-(heterocyclylmethyl)indoles as drugs. Macor, John Eugene; Wythes, Martin James (Pfizer Inc., USA). PCT Int. Appl. WO 9206973 A1 920430, 82 pp. DESIGNATED STATES: W: AU, BG, BR, CA, CS, DE, FI, HU, JP, KR, NO, PL, RO, SU, US; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, DE, DK, ES, FR, GA, GB, GR, IT, LU, ML, MR, NL, SE, SN, TD, TG. (English). CODEN: PIXXD2. APPLICATION: WO 91-US7194 911008. PRIORITY: US 90-597928 901015.
GI



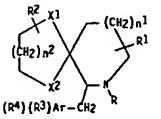
I

AB Title compds. I [n = 0-2; R2 = H, halo, cyano, R4O (wherein R4 = H, C1-6 alkyl, aryl), R6R5NCO(CH2)m, R6R5NSO2(CH2)m (wherein R5, R6 = H, C1-6 alkyl, aryl, C1-3 alkylaryl, R5R6 = 4-6-membered ring), R8CONR7(CH2)m R8SO2NR7(CH2)m (wherein R7, R8 = H, C1-6 alkyl, aryl, C1-3 alkylaryl), R8(O)xS(CH2)m, R6R5NCONR7(CH2)m, R9O2CNR7(CH2)m, R10(CH2)yCH:CH (wherein R9 = H, C1-6 alkyl, aryl, C1-3 alkylaryl, R10 = R6R5NCO, R6R5NSO2, R8CONR7, R8SO2NR7, etc.); m = 0-3; x = 1, 2; y = 0-2; R3 = H, alkyl], useful as 5-HT1 agonists, centrally acting antihypertensives, and vasodilators (no data) are prepd. (R)-3-[N-(Benzyloxycarbonyl)pyrrolidin-2-yl)carbonyl]-5-methoxy-1H-indole (prepn. given) was refluxed with LiAlH4 in THF to give (R)-I (R2 = MeO, R3 = Me, n = 1).
IT 143322-64-9
RL: RCT (Reactant)
(hydrogenation of, in prepn. of serotonin agonist)
IT 143322-46-7P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)
(prepn. and reaction of, in prepn. of indole deriv. drugs)
IT 143321-79-3P 143321-80-6P 143321-81-7P
143321-82-8P 143321-83-9P 143321-84-0P
143322-01-4P 143322-02-5P 143322-03-6P
143322-04-7P 143322-07-0P 143322-57-0P
143322-65-0P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)
(prepn. and reaction of, in prepn. of serotonin agonist)
IT 143321-58-8P 143321-72-6P 143321-73-7P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)
(prepn. and reaction of, in prepn. of serotonin agonist drug)
IT 5275-05-8P 101832-07-9P 143321-54-4P
143321-55-5P 143321-56-6P 143321-57-7P
143321-59-9P 143321-60-2P 143321-61-3P
143321-62-4P 143321-63-5P 143321-74-8P
143321-75-9P 143321-76-0P 143321-77-1P
143321-78-2P 143322-05-8P 143322-06-9P

L7 ANSWER 19 OF 21 CAPLUS COPYRIGHT 1996 ACS (Continued)
143322-10-5P 143322-11-6P 143322-12-7P
143322-13-8P 143322-14-9P 143322-15-0P
143322-16-1P 143322-17-2P 143322-18-3P
143322-19-4P 143322-20-7P 143322-21-8P
143322-22-9P 143322-23-0P 143322-24-1P
143322-25-2P 143322-26-3P 143322-27-4P
143322-28-5P 143322-29-6P 143322-30-9P
143322-31-0P 143322-32-1P 143322-33-2P
143322-34-3P 143322-35-4P 143322-36-5P
143322-37-6P 143322-38-7P 143322-39-8P
143322-40-1P 143322-41-2P 143322-42-3P
143322-43-4P 143322-44-5P 143322-45-6P
143322-47-8P 143322-48-9P 143322-49-0P
143322-50-3P 143322-51-4P 143322-52-5P
143322-53-6P 143322-54-7P 143322-55-8P
143322-58-1P 143322-59-2P 143322-60-5P
143322-61-6P 143322-62-7P 143322-63-8P
143322-67-2P 143322-68-3P 143322-69-4P
143322-71-8P 143393-07-1P 143393-09-3P
143577-59-7P 143577-60-0P 143577-61-1P
143577-63-3P
RL: BAC (Biological activity or effector, except adverse); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of, as drug)

L7 ANSWER 20 OF 21 CAPLUS COPYRIGHT 1996 ACS
1991:185267 Document No. 114:185267 Preparation of indoles and analogs as dopamine agonists and antihypertensives. Brubaker, Abram N. (Research Corp. Technologies, Inc., USA). U.S. US 4973593 A 901127, 17 pp. (English). CODEN: USXXAM. APPLICATION: US 87-81428 870804.

GI



I

AB The title compds. I (Ar = aryl, heteroaryl, etc.; R1 = H, alkyl, cycloalkyl, OH, alkoxy, etc.; R, R2 = H, alkyl, aryl; R3, R4 = H, alkyl, OH, alkoxy, amino, etc.; n1 = 0 or 1; n2 = 0-3; X1, X2 = O, CH, S, etc.) were prepd. I possess peripheral dopamine agonist activity and are devoid of any central dopamine stimulating activity. I are inactive at dopamine receptors in the brain. I are potent antihypertensives (no data). A mixt. of Et 6-[[4-(p-tolylsulfonyl)indolyl]methyl]-1,4-dioxa-7-azaspiro[4.5]decane-7-carboxylate and LiAlH4 in THF was refluxed for 12 h to give 6-(4-indolylmethyl-7-methyl-1,4-dioxa-7-azaspiro[4.5]decane, which exhibited ID50 of 0.095 mol/kg in the cat cardioaccelerator assay (CCA). (CCA is used for evaluation of dopamine agonist activity).

IT 133332-68-0P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)
(prepn. and reaction of, in prepn. of antihypertensive and peripheral dopamine agonist)

IT 133332-64-6P
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of, as antihypertensive and peripheral dopamine agonist)

L7 ANSWER 21 OF 21 CAPLUS COPYRIGHT 1996 ACS
1974:59926 Document No. 80:59926 1,2,4a,5,6,8,9,14,14a,14b-decahydrobenz[a]indolo(2,3-g]quinolizin-3(4h)-ones. Morrison, Glenn C.; Shavel, John, Jr. (Warner-Lambert Co.). U.S. US 3772306 731113, 3 pp. (English). CODEN: USXXAM. APPLICATION: US 71-202570 711126.

AB The title compd. (I) was prepd. by cyclizing 1,2,3,4-tetrahydro-1-(3-indolylmethyl)-6-methoxyisoquinoline with CH2O to give 5,6,8,9,14,14a-hexahydro-3-methoxybenz[a]indole[2,3-g]quinolizine, followed by oxidn. to 1,5,6,8,9,14,14a,14b-octahydrobenz[a]indolo[2,3-g]quinolizin-3(2H)-one and redn. of the 4,4a-double bond. I are antihypertensive.

IT 13118-20-2
RL: RCT (Reactant)
(reaction of, with formaldehyde)

L8 2 SEA FILE=CAPREVIEWS L4

L8 ANSWER 1 OF 2 CApreviews COPYRIGHT 1996 ACS
AN 95:656780 CApreviews
TI The in vivo pharmacological profile of a 5-HT1 receptor agonist, CP-122,288, a selective inhibitor of neurogenic inflammation
AU Gupta, P.; Brown, D.; Butler, P.; Ellis, P.; Grayson, K. L.; Land, G. C.; Macor, J. E.; Robson, S. F.; Wythes, M. J.; Shepperson, N. B.
CS Departments of Discovery Biology and Discovery Chemistry, Pfizer Central Research, Sandwich, Kent, CT13 9NJ, UK
SO Br. J. Pharmacol. (1995), 116(5), 2385-90
CODEN: BJPCBM; ISSN: 0007-1188
DT Journal
LA English
AB The aim of the present study was to investigate the in vivo pharmacol. profile of CP-122,288, an indole-deriv. with a conformationally restricted N-methylpyrrolidinyl basic side chain in the C-3 position. This C-3 substituent structurally differentiates CP-122,288 from the 5-HT1D receptor agonist sumatriptan, which possesses an N,N-dimethylaminoethyl group. When administered prior to elec. stimulation of the trigeminal ganglion, CP-122,288 (0.3-300 ng kg-1, i.v.) produced a dose-related inhibition of plasma protein extravasation in rat dura mater (min. ED, MED, 3 ng kg-1 i.v., P < 0.05; maximal inhibition of plasma extravasation at 30 ng kg-1 i.v., P < 0.01). Sumatriptan produced a similar inhibition of plasma leakage in the dura, but at much higher dose levels (MED, 100 .mu.g kg-1 i.v., P < 0.05). Thus, CP-122,288 is of the order of 104 fold more potent than sumatripan. At all doses tested, CP-122,288 did not inhibit plasma protein extravasation measured in extracranial tissues such as the lower lip, eyelid, and conjunctiva. In a sep. series of studies in the anesthetized rat, CP-122,288 (0.003-3 .mu.g kg-1 i.v.) produced no change in either heart rate or mean arterial blood pressure, thus demonstrating that doses of CP-122,288 which inhibit plasma protein leakage in rat dura, are devoid of hemodynamic effects. Following a 5 min period of elec. stimulation of the trigeminal ganglion, a 20 min period of sustained neurogenically-driven plasma extravasation, occurring in the absence of elec. stimulation, was initiated. By administration of the compd. 5 min after completing the phase of elec. stimulation, this protocol permitted the evaluation of the activity of CP-122,288 on the ongoing and established inflammatory event. CP-122,288 (30 and 300 ng kg-1, i.v. P <0.01 and P <0.05, resp.) produced a complete inhibition of plasma protein leakage which was consistent with its effects when administered prior to trigeminal ganglion stimulation. In the anesthetized dog, CP-122,288 and sumatriptan, at 1-300 .mu.g kg-1, i.v., produced a dose-dependent redn. in carotid arterial blood flow and coronary arterial diam. These data demonstrate that sumatriptan inhibits neurogenic inflammation in the rat (MED, 100 .mu.g kg-1, i.v.) and produces vasoconstriction in the dog, over a similar dose-range. Interestingly, doses of CP 122,288 that inhibit neurogenic inflammation in rat dura mater (0.3-300 ng kg-1) were demonstrated to be devoid of vasoconstrictor activity in either the carotid or coronary vascular beds of dog. These data demonstrate that in the rat, CP-122,288 is a highly potent and selective inhibitor of neurogenic inflammation in intracranial tissues, at doses which are devoid of vasoconstrictor activity in dog. Potentially, CP-122,288 may be of use for the acute treatment of migraine, without the risk of cardiovascular side-effects.

L8 ANSWER 1 OF 2 CApreviews COPYRIGHT 1996 ACS (Continued)

L8 ANSWER 2 OF 2 CApreviews COPYRIGHT 1996 ACS
AN 95:538604 CApreviews
TI Preparation of triazole derivatives as serotoninergic agonists
IN Matassa, Victor Giulio; Sternfeld, Francine; Street, Leslie Joseph
PA Merck Sharp and Dohme Ltd., UK
SO PCT Int. Appl., 49 pp.
CODEN: PIXXD2
PI WO 9521166 A1 950810
DS W: AM, AT, AU, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, JP, KE, KG, KP, KR, KZ, LK, LR, LT, LU, LV, MD, MG, MN, MW, MX, NL, NO, NZ, PL, PT, RO, RU, SD, SE, SI, SK, TJ, TT, UA, US
RW: KE, MW, SD, SZ, AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG
AI WO 95-GB134 950124
PRAI GB 94-2016 940202
DT Patent
LA English
AB Triazole derivs. represented by formula (IIA), and salts and prodrug thereof, wherein R1 represents C1-6 alkoxy(C1-6)alkyl, C2-6 alkenyl, C2-6 alkynyl, C3-7 cycloalkyl, C3-7 cycloalkyl(C1-6)alkyl, aryl, aryl(C1-6)alkyl, aryloxy(C1-6)alkyl, aryl(C2-6)alkenyl, aryl(C2-6)alkynyl, C3-7 heterocycloalkyl(C1-6)alkyl, heteroaryl, heteroaryl(C1-6)alkyl, heteroaryl(C2-6)alkenyl or heteroaryl(C2-6)alkynyl, any of which groups may be optionally substituted; are selective agonist of 5-HT1-like receptors and are therefore useful in the treatment of clin. conditions, in particular migraine and assocd. disorders, for which a selective agonist of these receptors is indicated.

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L9            1 SEA FILE=REGISTRY 143321-74-8/RN

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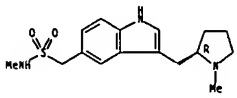
L9 ANSWER 1 OF 1 REGISTRY COPYRIGHT 1996 ACS
RN 143321-74-8 REGISTRY
CN 1H-Indole-5-methanesulfonamide, N-methyl-3-[(1-methyl-2-pyrrolidinyl)methyl]-, (R)- (9CI) (CA INDEX NAME)
OTHER NAMES:
CN CP 122288
FS STEREOSEARCH
MF C16 H23 N3 O2 S
SR CA
LC STN Files: CA, CANCERLIT, CAPLUS, CAPREVIEWS, CASREACT, CHEMINFORMRX, MEDLINE, TOXLIT
DES 1:R

Absolute stereochemistry.



1 REFERENCES IN FILE CAPREVIEWS
8 REFERENCES IN FILE CA (1967 TO DATE)
8 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 124:688

REFERENCE 2: 122:306133

REFERENCE 3: 122:256183

REFERENCE 4: 122:205025

REFERENCE 5: 122:64328

REFERENCE 6: 119:262341

REFERENCE 7: 118:168927

REFERENCE 8: 117:171215